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PREGNANCY FOLLOWING LUMBODORSAL SPLANCHNICECTOMY FOR ESSENTIAL AND MALIGNANT HYPERTENSION AND HYPERTENSION ASSOCIATED WITH CHRONIC PYELONEPHRITIS

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BOSTON

THE prognosis in pregnancy complicated by a pre-existing hypertension with or without renal disease is notoriously poor for both the mother and the infant. Corwin and Herrick,[1, 2] in their classic papers written in 1927, made the following statement:

> Very few women who begin pregnancy with a blood pressure above 150 systolic or 100 diastolic can go through pregnancy successfully, that is with a living child. It is our opinion moreover, that pregnancy does much to accelerate the progress of chronic cardiovascular disease, that it may bring it out when latent and is to be avoided when the disorder has made evident inroads.

Severe hypertension of any origin is considered by many others to be a strong indication for therapeutic abortion. Watson[3] regarded a pronounced hypertension with or without albuminuria as an indication for the induction of abortion. Fishberg[4] observed that the pregnancy should be terminated if the blood pressure continued to rise or evidence of cardiac or renal insufficiency appeared.

In the 14 cases reported below all the patients had arterial hypertension, the blood pressures averaging 196 systolic, 130 diastolic, on admission prior to splanchnicectomy. For the most part the prenatal care and deliveries were conducted by obstetricians in the localities in which the patients resided. The blood-pressure reactions were studied by the postural and cold test in the first trimester and in most cases at seven months of pregnancy and at six weeks post partum.

As might have been expected with this type of case, the average age at delivery was thirty-one years. The average parity was 2.3. The time elapsing between the diagnosis of hypertension and the splanchnicectomy averaged seventy-five months, and the time between splanchnicectomy and the pregnancy studied averaged thirty-one months, with the exception of a case in which splanchnicectomy was performed during the first trimester. The blood pressure following splanchnicectomy prior to the pregnancies averaged 135 systolic, 87 diastolic, and only 2 patients had persistent albuminuria.

The nature of the hypertension is of interest. Seven patients were classified preoperatively as having so-called "essential hypertension." Three gravida I's and 2 gravida II's, all without demonstrable kidney disease, were known to have had hypertension prior to their pregnancies. One gravida III and 1 gravida V, also without demonstrable kidney disease, developed hypertension during the second and first pregnancies respectively. Two gravida I's and 2 gravida II's were classified as having essential hypertension and associated chronic pyelonephritis, the presence of the latter being proved by renal studies, by gross inspection of the kidneys at operation and by biopsies taken from the kidneys. Two gravida II's developed both hypertension and pyelonephritis during the first pregnancies. The 2 remaining patients in this group developed renal disease and hypertension prior to their pregnancies. There were 3 cases of malignant hypertension, with pyelonephritis in 2. In a gravida II the disease began two years after the first pregnancy; another gravida II had had eclampsia during her first pregnancy six years earlier and known hypertension for two years, and in a gravida V the disease had become manifest during her third pregnancy. Thus, in all cases, hypertension antedated the pregnancies under discussion, and in 3 cases previous pregnancies had been interrupted because of hypertension.

In 9 cases the blood pressure during pregnancy remained within normal limits, and there was no albuminuria. The other 5 patients showed no significant elevation of blood pressure until the third trimester, when 2 developed marked elevation (above 180 systolic). In one of these cases a

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++++ test for albumin necessitated interruption of the pregnancy at the thirty-fourth week. Three cases showed only moderate hypertension (blood pressures below 160 systolic, 90 diastolic), but 1 of these patients, who had developed a premature separation of the placenta in her first pregnancy, successfully completed her second pregnancy after the termination of the study. In this group there were normal deliveries in 11 cases and cesarean sections in 3, the indication being a previous hysterotomy in 2 cases and fulminating pre-eclampsia in another. Thirteen babies are living and well — 2 were delivered prematurely. One infant was stillborn owing to premature separation of the placenta. The puerperium was uncomplicated in all cases except for the patient in Case 11, who developed a post-partum psychosis. The average blood pressure was 134 systolic, 89 diastolic, at two weeks post partum and 133 systolic, 87 diastolic, at six or more weeks post partum. None of the patients had albuminuria at that time.

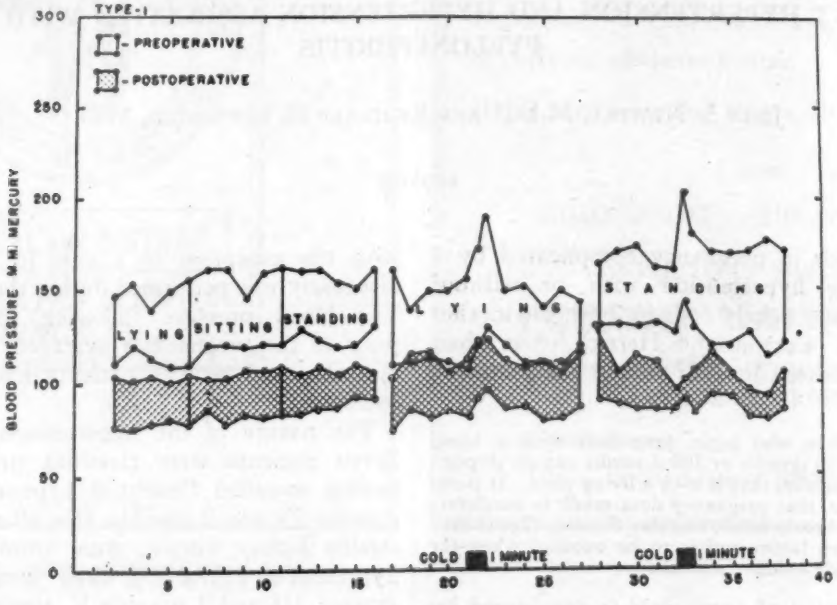

FIGURE 1. *Case 1.*

This chart shows the blood-pressure levels before lumbodorsal splanchnicectomy and ten months later, one month after delivery. The postural and "cold" blood-pressure readings are compared. In recording these, readings are taken every minute for five minutes with the patient lying, sitting and standing. A cold test is then performed with the patient lying and is repeated with the patient standing. The postoperative (post-partum) range is shaded. This patient was six weeks pregnant when the splanchnicectomy was performed.

The following are brief abstracts of the case reports:

CASE 1. A 24-year-old gravida II had first been seen in the 9th month of her first pregnancy with a blood pressure of 168/110 but no albuminuria. The blood pressure remained in this range for the remainder of this pregnancy, and the patient was delivered at term of a living infant. She was next seen 3 years later with a blood pressure of 186/120. The blood pressure continued to rise during the next 6 months, when she was admitted to the hospital. At that time the patient was 6 weeks pregnant. The consultant from the hypertensive clinic and the obstetric consultant believed that the conservative and wisest procedure was to terminate this pregnancy. In view of our previous experience with pregnancy following splanchnicectomy, however, the consultants agreed to postpone abortion until the results of the splanchnicectomy could be determined, since in our opinion this latter procedure was indicated regardless of the pregnancy.* The family history revealed that the patient's mother had died of kidney disease.

The blood pressure on admission was 180/120, and the range during postural and cold tests was 138/106 to 204/144. The eye grounds were normal. A 7-foot heart plate was consistent with hypertension. An electrocardiogram and the nonprotein nitrogen were normal. A phenolsulfonephthalein test showed 45 per cent excretion of the dye in 15 minutes and 65 per cent in 2 hours. The urine concentrated to 1.020 and contained no albumin, and the sediment was normal, as was an intravenous pyelogram. On sedation the blood pressure fell to 120/50. The Aschheim–Zondek test was positive.

On July 1, 1944, the first stage of a bilateral lumbodorsal splanchnicectomy was performed, with removal of the sympathetic trunk from the eighth dorsal to the third lumbar segment inclusive. Two weeks later a similar operation was performed on the left side, with removal of the sympathetic trunk from the eighth dorsal to the second lumbar inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. Renal biopsies revealed chronic vascular nephritis, Grade II. The patient experienced an uneventful convalescence, and at discharge the blood pressure was 110/80.

During the remainder of this pregnancy the blood pressure was 110/70 to 104/90. There were no signs or symptoms of toxemia, and the urine was consistently free of albumin. On January 24, 1945, the patient was delivered of a living infant. The blood pressure during the puerperium varied between 102/60 and 130/100. At two subsequent post-partum visits the blood pressure was 128/78 and 132/80. Three months post partum the blood pressure was 120/80, and a month later it was 102/78. Blood-pressure data as revealed by the postural and cold tests are presented in Figure 1.

*In general we believe that the best results are obtained when the pregnancy follows the splanchnicectomy by at least twelve months. There may be a group of patients, such as this one, however, in whom operation could be performed in the first trimester.

Case 2. This patient was 20 years of age at the time of her final admission in November, 1940. At the age of 4 she had been admitted for a urinary-tract infection and had subsequently been followed in the Out Patient Department. During the 3 years prior to splanchnicectomy she had been admitted to the hospital twice because of urinary-tract infections caused by an organism of the colon-bacillus group. This infection responded to chemotherapy, and the urine became intermittently sterile. The blood pressure had always been elevated, and during this period the hypertension became progressively severer and the eye-ground changes progressively more marked. The family history was noncontributory.

On final admission the blood pressure was 205/140, and the range during postural and cold tests was from 205/150 to 174/135. The eye grounds showed Grade II changes, both spastic and sclerotic. The heart was normal in size and slightly altered in shape. The nonprotein nitrogen was 26 mg. per 100 cc.; a phenolsulfonephthalein test showed 15 per cent excretion of the dye in 15 minutes and 50 per cent in 2 hours. The maximum urinary concentration was 1.012. There was a ++ test for albumin, and the sediment contained a few to many white cells. Cultures of the urine showed abundant growth of nonhemolytic streptococci. Intravenous pyelograms were not remarkable. On sedation the blood pressure fell to 145/100.

On November 20 the first stage of a lumbodorsal splanchnicectomy was performed, the sympathetic trunk on the left being removed from the tenth dorsal to the second lumbar segment inclusive. The second stage was performed on December 3, the sympathetic trunk being removed from the tenth dorsal to the first lumbar inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. At operation both kidneys were found to be irregularly scarred, contracted and lobulated, a finding typical of chronic pyelonephritis. Biopsies taken from both kidneys showed typical chronic pyelonephritis and chronic vascular nephritis, Grade III. The patient was discharged on December 16, the blood pressure being 133/104. Two years after the splanchnicectomy the blood pressure was 109/82.

The patient became pregnant for the first time 3½ years after operation, the blood pressure being 128/94 and the urine containing no albumin. During the 6th month of pregnancy the blood pressure was 122/88, but at 34 weeks a blood pressure of 170/110 developed and the urine showed a ++++ test for albumin. She was delivered by cesarean section of an infant weighing 3 pounds, 9 ounces, who survived. Two months post partum and 51 months after operation the blood pressure was 138/94.

Case 3. A 28-year-old gravida I was admitted in May, 1942, for hypertension. For 15 years she had had headaches associated with vomiting. Nine years previously she was found to have a slightly elevated blood pressure, and 18 months prior to admission the blood pressure was 180/120. Both parents, who were 49 and 56 years of age, had hypertension.

The blood pressure on admission was 180/130, the range during postural and cold tests being 198/140 to 148/88. The retinal vessels showed spasm. The heart was normal in size and shape. An electrocardiogram was within normal limits. The nonprotein nitrogen was 26 mg. per 100 cc. A phenolsulfonephthalein test showed 32 per cent excretion of the dye in 30 minutes and 65 per cent in 2 hours. The urine, which concentrated to 1.026, gave a + test for albumin, and the sediment contained 10 white cells per high-power field. On June 1 the first stage of a lumbodorsal splanchnicectomy was performed, with removal of the sympathetic trunk from the ninth dorsal to the third lumbar segment, inclusive, on the right. Two weeks later, at a similar operation, the sympathetic trunk on the left side was removed from the ninth dorsal to the second lumbar inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. Biopsies of the kidney were reported as showing a chronic vascular nephritis, Grade II. After an uneventful convalescence the patient was discharged with a blood pressure of 140/100.

In August, 1943, she became pregnant. The pregnancy was uneventful, the blood pressure varying between 120/84 and 185/120 and the urine remaining free of albumin. At the 35th week of pregnancy she was checked at the hypertension clinic and found to have a blood pressure of 138/90. Three hours later she experienced massive vaginal bleeding.

On admission to the hospital the blood pressure was 180/120, and the urine gave a +++ test for albumin. The uterus was firm and did not relax. A diagnosis of premature separation of the placenta was made. Since the fetal heart beat disappeared 20 minutes after admission, the membranes were ruptured and labor was stimulated with minimal doses of Pitocin. Ten hours later a stillborn, premature infant was delivered by low forceps. The placenta was completely separated, and the uterus was filled with large blood clots. The patient suffered moderate shock and required two transfusions during labor. She was discharged on the 13th postpartum day, when the blood pressure was 148/98.

The patient experienced a second pregnancy, which terminated successfully in March, 1945, with a normal delivery of a living infant weighing 4 pounds, 4 ounces. This delivery was also complicated by premature separation of the placenta. During pregnancy the blood pressure averaged 155/105, and the urine remained free of albumin. Labor was painless until the head distended the perineum.

Case 4. A 28-year-old gravida I had first been known to have hypertension when she was 13 years old. The blood pressure at times was recorded as over 200 systolic. The admission blood pressure was 205/150, the range during postural and cold tests being 205/154 to 148/110. The eye grounds were classified as Grade I. A 7-foot plate showed the heart to be normal in size and shape. The electrocardiogram was normal. The nonprotein nitrogen was 28 mg. per 100 cc. A phenolsulfonephthalein test showed 30 per cent excretion of the dye in 15 minutes and 93 per cent excretion in 2 hours. The urine, which concentrated to 1.022, gave a + test for albumin; the sediment was normal, as was an intravenous pyelogram. On sedation the blood pressure fell to 138/110.

In February, 1944, the first stage of a bilateral lumbodorsal splanchnicectomy was performed, the left sympathetic trunk being removed from the eighth dorsal to the first lumbar segment, inclusive. Two weeks later the second stage was performed, the right sympathetic trunk being removed from the seventh dorsal to the second lumbar inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. A renal biopsy showed a chronic vascular nephritis, Grade III.

Three months later, when the patient became pregnant, the blood pressure was 140/100, and the urine was normal. At 7 months the sediment contained white cells in clumps. This cleared with sulfadiazine therapy. At 34 weeks the blood pressure was 160/104, and 2 weeks later it rose to 190/128. The patient remained at bed rest in the hospital until the 40th week of pregnancy, when she started in labor spontaneously and was delivered normally of a living infant. For the 4 weeks prior to delivery while at bed rest she had had no complaints, and the urine had remained free of albumin. The blood pressure varied widely, averaging 170/120. On several occasions it reached 180/130, but a few hours later was found to be 126/90. Following delivery the blood pressure continued to be labile and was 170/110 when the patient was discharged. Eight months post partum the reading was 106/96 with the patient in the horizontal position. It could be raised to 160/118 when she was standing and stimulated by cold.

Case 5. A 28-year-old gravida II was admitted in May, 1942, with a diagnosis of malignant hypertension. Ten years previously she had experienced a normal pregnancy. Three years later she began having headaches, which became progressively severer.

The blood pressure on admission was 245/140, the range during postural and cold tests being 250/170 to 196/132. The eye grounds showed hypertensive retinopathy with papilledema. A 7-foot heart plate showed definite enlargement. The heart was altered in shape, and the aorta was tortuous. An electrocardiogram was consistent with hypertensive heart disease. The nonprotein nitrogen was 33 mg. per 100 cc. A phenolsulfonephthalein test showed 15 per cent excretion of the dye in 15 minutes and 15 per cent in 2 hours. The urine showed a specific gravity of 1.012, with a ++ test for albumin, and the sediment contained rare red cells. Intravenous pyelograms were normal. On sedation the blood pressure fell to 150/110.

On May 9 the first stage of a lumbodorsal splanchnicectomy was performed, the right sympathetic trunk being removed from the ninth dorsal to the second lumbar segment, inclusive. The same operation was repeated on the left side two weeks later. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. At operation the kidneys were noted to be scarred and contracted in an irregular fashion. Renal biopsies showed a Grade II chronic vascular nephritis on the left and a Grade III on the right. The patient was discharged on June 17, the blood pressure being 137/116.

Fourteen months after operation she was readmitted for study. Nausea and occasional dyspnea were the only symptoms. The blood pressure on admission was 132/90, the range during postural and cold tests being 158/110 to 120/106. A phenolsulfonephthalein test showed 55 per cent excretion of the dye in 2 hours. The nonprotein nitrogen was 16 mg. per 100 cc., and the urine showed a specific gravity of 1.016 and a + test for albumin. In addition to the marked improvement in the blood pressure the heart had decreased in size, and the electrocardiogram showed a striking improvement with return to normal of the ST segments and T waves. The eye grounds showed minimal residual changes and were classified as Grade I.

The patient had become pregnant 1 year after operation. The pregnancy was uneventful, and she was delivered at term of a living infant, the blood pressure rising to 160/110 during labor (Fig. 2).

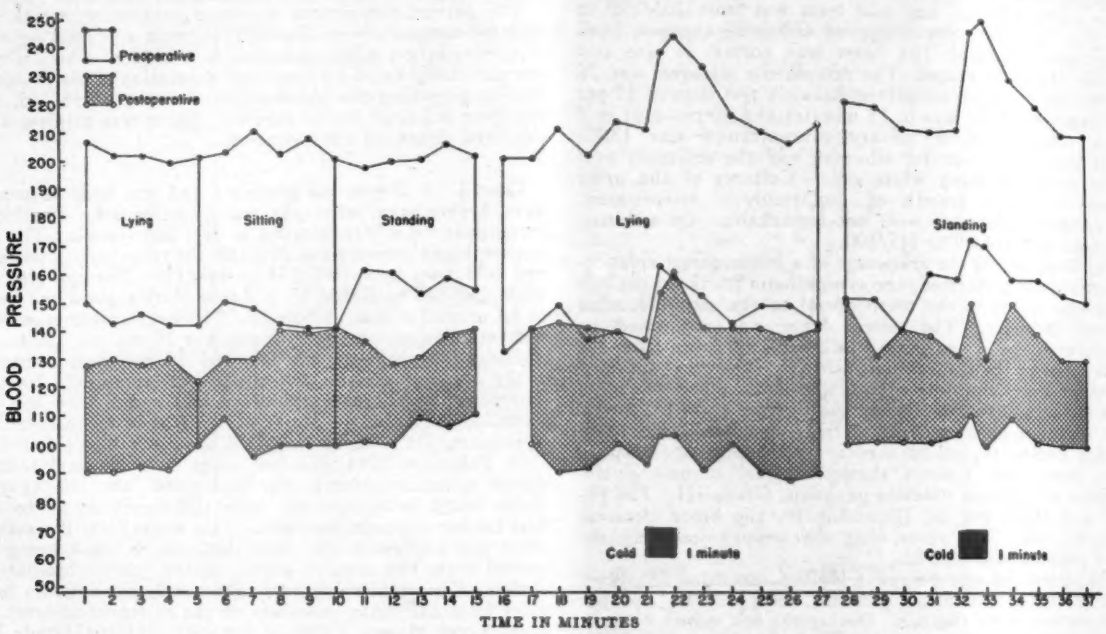

FIGURE 2. *Case 5.*

The blood-pressure readings before lumbodorsal splanchnicectomy for malignant hypertension, associated with chronic bilateral pyelonephritis, are compared with those made fourteen months later (range shaded), at which time the patient was in the second month of pregnancy, whose subsequent course was uneventful.

CASE 6. A 29-year-old gravida II had first been seen in March, 1937, at the age of 20 years. She had had known hypertension since her 12th year. During childhood she had had kidney trouble, the details of which were not known. For the previous eight years the blood-pressure range had been 182/112 to 240/116. The symptoms consisted of headaches of increasing severity, nervousness, vertigo and increasing fatigability.

The blood pressure on admission was 170/120, the range during postural and cold tests being 176/116 to 240/160. A 7-foot plate showed the heart to be normal in size and shape. The electrocardiogram was normal, as were the eye grounds. The nonprotein nitrogen was 24 mg. per 100 cc. A phenolsulfonephthalein test showed 25 per cent excretion of the dye in 15 minutes and 62 per cent in 2 hours. The maximum urinary concentration was 1.027, with a + test for albumin, and the sediment was normal. Intravenous pyelograms were normal. On sedation the blood pressure fell to 132/90.

On April 1 the first stage of a splanchnicectomy* was performed, the left sympathetic trunk being excised from the tenth dorsal to the twelfth dorsal segment, inclusive. The same operation was performed on the right side 10 days later. The great splanchnic nerves were removed from the celiac ganglions to the midthoracic level. The patient was discharged on April 22 with a blood pressure of 115/86. She was seen at intervals during the next 4 years. The postoperative blood pressures were as follows: at 2 months, 120/80; at 5 months, 110/80; at 16 months, 108/80; at 24 months, 110/80; at 27 months, 129/90; at 42 months, 126/94; and at 50 months, 122/85.

The patient first became pregnant during the 6th year after operation. She was followed in this pregnancy through the 26th week; the blood pressure did not exceed 104/60, and the urine was normal. The patient was not seen for the remainder of this pregnancy, which resulted in a stillbirth, the details of which are not known.

The patient was next seen 8 years after operation during her second pregnancy, when she was 29 years old. The blood pressure during this pregnancy was as follows: at 4 months, 112/64; at 5 months, 100/70; at 6 months, 114/80; at 7 months, 110/60; and at 8 months, 126/68. The urine was negative for albumin throughout this pregnancy. A 7-pound female infant was delivered spontaneously on July 7, 1945. Six and 11 weeks post partum the blood pressures were 136/88 and 120/82 respectively.

CASE 7. A 29-year-old gravida I was first seen in 1938, when she was 24 years of age and single. Seven years previously, during a routine physical examination, an elevation

*In this case and in Case 10, a lower thoracic sympathectomy and splanchnicectomy were performed. These patients were operated on prior to October, 1938, when lumbodorsal splanchnicectomy was adopted as routine for hypertension. These were 2 of a few excellent results that one of us (R. H. S.[9]) has noted following this operation for hypertension. Peet[8] reported the case of a patient with malignant hypertension who responded well to an operation of this type. The blood pressure of his 22-year-old patient prior to operation ranged from 230/170 to 280/190. Eight months later it was 136/90. The patient became pregnant 14 months after operation. Two months later the blood pressure rose to nearly preoperative levels, and an abortion was performed. Four years and two months after operation the patient was well, and the blood pressure was 139/101.

of blood pressure was detected. A year later the patient lost 25 pounds and suffered headaches that became worse during the 2 or 3 years preceding admission.

The blood pressure on admission was 225/130, the range during postural and cold tests being 226/146 to 184/114. The eye grounds were classified as Grade II. A 7-foot plate showed the heart to be normal in size and slightly altered in shape, the aorta being slightly tortuous. An electrocardiogram was normal. The nonprotein nitrogen was 26 mg. per 100 cc. and a phenolsulfonephthalein test showed 32 per cent excretion of the dye in 15 minutes and 55 per cent in 2 hours. The urine concentrated to 1.019, gave a + test for albumin and contained a slightly abnormal sediment. Intravenous pyelograms were normal. On sedation the blood pressure fell to 122/80.

On November 22 the first stage of a lumbodorsal splanchnicectomy was performed. The sympathetic trunk was removed from the second dorsal to the first lumbar segment, inclusive. At a similar operation 2 weeks later, the right trunk was removed from the ninth dorsal to the first lumbar. The great splanchnic nerves were removed from the celiac ganglions to the midthoracic level. The patient was discharged on December 13, the blood pressure ranging between 152/104 and 166/114.

She was readmitted for study in March, 1942, at which time she had no complaints. The blood pressure was 150/90 on admission but dropped to 110/94 with bed rest, the range being 150/90 to 80/40. The eye grounds were classified as Grade II. The cardiac status was considered normal. The renal blood flow (as measured by the Diodrast-clearance method) was 640 cc. per minute, or about two thirds normal.

The patient became pregnant in 1943. This pregnancy was uneventful throughout, with no signs or symptoms of toxemia and with delivery of a living infant at term. Two months post partum (62 months after operation) the patient was studied again. The blood pressure on admission was 132/82, and the range was from 164/114 to 128/88. An electrocardiogram and the kidney-function tests were normal, and the eye grounds were completely normal.

Case 8. A 31-year-old gravida III was first seen at the age of 29 years. She complained of severe headaches of 7 years' duration and had had known hypertension for 6 years. The family history was strongly positive for hypertensive disease. One year prior to admission she was delivered of a living child, the pregnancy being induced at 36 weeks because of a blood pressure of 230/120 and albuminuria. The puerperium was complicated by pyelitis. Four months before admission a therapeutic abortion had been performed.

On admission the blood pressure was 150/100, the range during postural and cold tests being 124/90 to 150/116. The heart was normal in size and shape, and the aorta was not tortuous. An electrogram was normal, and the eye grounds were reported as showing Grade I changes. The specific gravity of the urine was 1.018, and there was no albumin; the sediment was normal. The nonprotein nitrogen was 20 mg. per 100 cc. Intravenous pyelograms were normal except that there was slight evidence of pyelonephritis on the right side. On sedation the blood pressure fell to 110/78.

On March 19, 1943, the left sympathetic trunk was removed from the eighth dorsal to the second lumbar segment inclusive. On April 4 the right sympathetic trunk was removed from the ninth dorsal to the second lumbar inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. Biopsies of the kidneys were reported as showing a Grade I chronic vascular nephritis on the right and a Grade II chronic vascular nephritis on the left.

The patient became pregnant 27 months after operation. At that time the blood pressure was 138/80, and the urine negative for albumin. The pregnancy was entirely normal throughout, the blood-pressure range being 120/78 to 140/90 and the urine consistently negative for albumin. An infant weighing 6 pounds, 3 ounces, was delivered normally in March, 1946, after a short painless labor. Two weeks post partum the blood pressure was 120/80, and the urine normal.

Case 9. A 32-year-old gravida III was admitted in March, 1942, for hypertension. Nineteen months previously she had consulted a physician for prenatal care and had been found to have a systolic blood pressure of 200. Headache was the prominent symptom during this pregnancy, which terminated normally at term. Headache and tinnitus had subsequently persisted. The first pregnancy, 10 years previously, was believed to have been normal. The patient's mother had hypertension, and her father had died of a cerebral accident.

The blood pressure on admission was 190/110, the range during postural and cold tests being 190/140 to 158/102. The eye grounds showed narrowing of the retinal arteries. A 7-foot plate revealed the heart to be slightly altered in size and shape and the aorta to be tortuous. An electrocardiogram was within normal limits. The nonprotein nitrogen was 18 mg. per 100 cc., and a phenolsulfonephthalein test showed 15 per cent excretion of the dye in 15 minutes and 75 per cent in 2 hours. The urine concentrated to 1.028 and gave a ++ test for albumin, and the sediment showed rare red cells. Intravenous pyelograms showed prompt excretion and normal kidneys. On sedation the blood pressure fell to 128/90.

On March 23 the first stage of a bilateral lumbodorsal splanchnicectomy was performed on the right, the sympathetic trunk from the ninth dorsal to the third lumbar segment, inclusive, being excised. An identical operation was performed on the left 2 weeks later. The great splanchnic nerves were removed from the celiac ganglions to the midthoracic level on both sides. Reports of the biopsies from the kidneys revealed a Grade III chronic vascular nephritis.

The patient became pregnant in July, 1943, and was readmitted in October for study and for a decision regarding the advisability of abortion. She complained of easy fatigability and nocturnal dyspnea. The blood pressure was 155/105 on admission, but became normal during the hospital stay. The urine concentrated to 1.030 and gave a + test for albumin, and the sediment contained occasional white cells. A phenolsulfonephthalein test showed 65 per cent excretion of the dye in 2 hours, and the nonprotein nitrogen was 20 mg. per 100 cc. It was decided that the pregnancy should be allowed to continue. The course of the pregnancy was uneventful, the blood pressure remaining below 155/100; the urine gave a + test for albumin or less. A female infant weighing 7 pounds, 10 ounces, was delivered on March 10, 1944, following a normal labor.

Case 10. A 34-year-old gravida II had first been seen in May, 1936, when she was 25 years old and single. Her complaints were headache and loss of vision. For 8 years she had had headaches that had become progressively severer. Eighteen months prior to admission she had been refused life insurance because of a systolic blood pressure of 170. The amaurosis had been present for 2 weeks. The patient's mother had died of cerebral hemorrhage, and an aunt of hypertensive disease.

The blood pressure on admission was 230/140. The heart was enlarged and abnormal in size and shape. An electrocardiogram showed slight changes, with left-axis deviation. The eye grounds were classified as Grade III and showed albuminuric retinitis. The patient could not distinguish fingers at 3 feet. The nonprotein nitrogen was 25 mg. per 100 cc. A phenolsulfonephthalein test showed 18 per cent excretion of the dye in 15 minutes and 56 per cent in 2 hours. The urine concentrated to 1.016 and showed a ++ test for albumin, and the sediment contained white cells in clumps and an occasional granular cast. The uterus was consistent with a 7½ months' pregnancy. The pregnancy was interrupted by an abdominal hysterotomy, a normal living female infant weighting 4 pounds, 8 ounces, being delivered.

Three months later the blood pressure was 158/100, and this dropped to 140/90 with bed rest. The urine concentrated to 1.016 and gave a ++++ test for albumin, and the sediment contained hyaline and granular casts.

In December the patient was readmitted with a blood pressure of 165/110. A two-stage operation was performed, the sympathetic trunk from the tenth to the twelfth dorsal segment, inclusive, being removed on each side. The great splanchnic nerves were removed on both sides from the celiac ganglions to the mid-thoracic level. The convalescence was uneventful.

Six years later the patient became pregnant for the second time. The blood pressure during the pregnancy varied between 140/80 and 120/80. The patient was symptom free and in good health throughout. The urine was free of albumin until the 7th month, when it gave a + test for albumin and the sediment showed white cells in clumps, which however, responded to sulfadiazine therapy. Two weeks prior to term

the patient was delivered by a repeat hysterotomy of a female infant weighing 6 pounds, 5 ounces. The puerperium was uneventful. Six weeks post partum the blood pressure was 136/88, and the urine was free of albumin.

CASE 11. A 33-year-old gravida II was admitted in September, 1940, with the diagnosis of malignant hypertension and pyelonephritis. She had been known to have hypertension for 2 years. The family history was irrelevant. Six years before admission, in the 8th month of the first pregnancy, pyelitis, hypertension, coma and convulsions had developed. This pregnancy had been terminated by an abdominal hysterotomy at the 36th week. For 2 years prior to admission the patient had had frequent headaches, tinnitus and transient paresthesias.

The blood pressure on admission was 240/150, the range during postural and cold tests being from 138/112 to 240/150. The heart was normal in size and shape. An electrocardiogram was typical of hypertension. The eye grounds showed marked hypertensive changes with hemorrhages, exudate and advanced changes in the retinal arteries and marked bilateral papilledema. The nonprotein nitrogen was 21 mg. per 100 cc., and a phenolsulfonephthalein test showed 25 per cent excretion of the dye in 15 minutes and 55 per cent in 2 hours. The maximum urine concentration was 1.030. There was a + test for albumin, and the sediment was normal. Intravenous pyelograms were normal. On sedation the blood pressure fell to 126/98.

The first stage of the splanchnicectomy was performed on October 2. The left sympathetic trunk was excised from the ninth dorsal to the second lumbar segment, inclusive. At the second stage, on October 16, the right sympathetic trunk was removed from the ninth dorsal to the first lumbar, inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. No biopsies were taken, but at operation both kidneys were described as diffusely scarred and contracted in an irregular fashion, the gross appearance being characteristic of chronic pyelonephritis. The patient was discharged on October 30, when the blood pressure was 124/95.

Twenty-seven months after operation the blood pressure was 124/91, the range during postural and cold tests being 140/108 to 112/82. Eleven months later the blood pressure was 120/76, and the range 150/112 to 115/68. Fifty-five months postoperatively, when the patient was 1 month pregnant, the blood pressure was 98/58, and the urine was normal. The pregnancy was entirely uneventful. The blood-pressure range was 115/80 to 150/98. The urine remained free of albumin, and the total weight gain was 17 pounds.

Sixty-four months after operation, when the patient was 2 weeks from term, a repeat hysterotomy was performed under spinal anesthesia. A female infant weighing 7 pounds was delivered. The surgical convalescence was uneventful, and the patient was discharged on the 14th postoperative day, the blood pressure being 120/84 and the urine free of albumin. Unfortunately, the patient manifested symptoms of a puerperal psychosis beginning on the 10th post-partum day. These symptoms increased in severity so that after a short stay at home she was institutionalized.

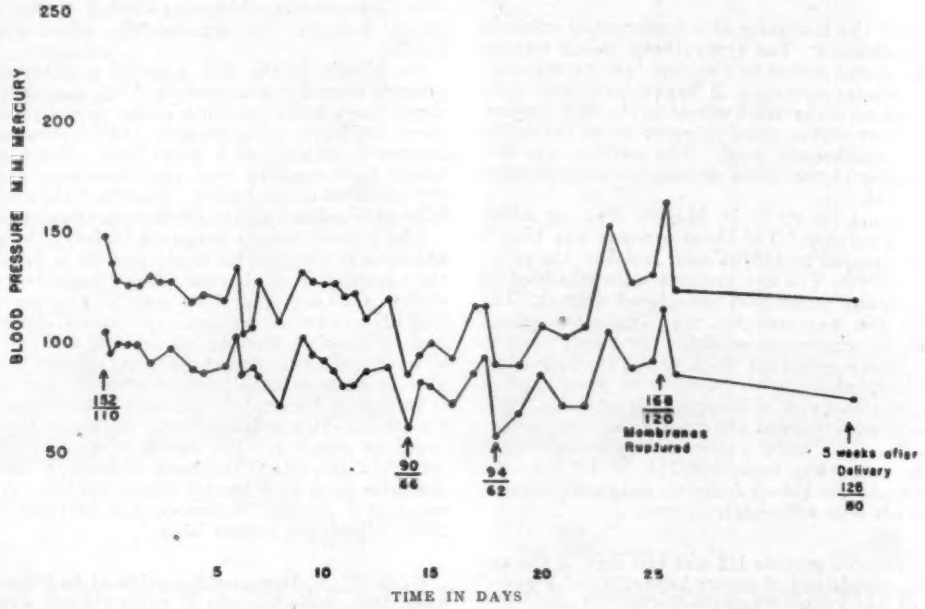

FIGURE 3. *Case 12.*

The average blood-pressure levels are charted for twenty-six days prior to delivery. During that time the patient was hospitalized because of a reading of 152/110. She responded well to rest. The membranes were ruptured ten days prior to term because the blood pressure had risen to 168/120. Five weeks following delivery the level was 125/80. This patient had malignant hypertension prior to lumbodorsal splanchnicectomy.

CASE 12. A 36-year-old gravida V was admitted in February, 1941, with a diagnosis of malignant hypertension which had developed during the third pregnancy in 1935. The fourth pregnancy had been interrupted at 4 months because of severe hypertension.

The blood pressure on admission was 206/130, the range during postural and cold tests being 164/110 to 220/160. The eye grounds showed changes indicative of the malignant phase of hypertensive disease. There were marked abnormalities of the retinal arteries, with occasional hemorrhages and associated papilledema. A 7-foot plate showed the heart to be enlarged and abnormal in shape, with a tortuous aorta. An electrocardiogram was consistent with mild hypertensive heart disease. The nonprotein nitrogen was 15 mg. per 100 cc., and a phenolsulfonephthalein test showed 40 per cent excretion of the dye in 15 minutes and 75 per cent in 2 hours. The urine contained no albumin, and the sediment was normal, as were intravenous pyelograms.

On February 25, 1941, at the first stage of a lumbodorsal splanchnicectomy the sympathetic trunk from the tenth dorsal to the first lumbar segment, inclusive, was removed on the right. Two weeks later, at the second stage, the left sympathetic trunk from the ninth dorsal to the first lumbar, inclusive, was removed. Biopsies from both kidneys showed a chronic Grade II vascular nephritis. After a normal convalescence the patient was discharged on March 29, with a blood pressure of 135/95.

She was next seen in June, 1942, when she was 24 weeks pregnant. At that time a Diodrast-clearance test showed a marked reduction in renal blood flow to about a third of normal. The blood pressure was 132/92, and the urine was normal. The pregnancy continued uneventfully until the 34th week, when the blood pressure rose to 152/110 and the weight had increased to 234 pounds. The patient was admitted to the Boston Lying-in Hospital for study. The blood pressure responded well to bed rest (Fig. 3). The urea clearances during the 37th week of pregnancy showed 99 per cent and 104 per cent excretion of the dye respectively. During the following week the blood pressure rose to 164/120, and the urine showed a ++ test for albumin. Labor was induced by rupture of the membranes, and an infant weighing 6 pounds, 5 ounces, was delivered normally. Two and 6 weeks post partum the blood pressure was 110/84 and 122/84 respectively. The patient was evaluated 3 months after delivery, when the blood pressure was 120/68, the range during postural and cold tests being 110/80 to 150/130. When she was admitted for study 34 months later the blood pressure was 178/118, the range being 146/110 to 210/164. The eye grounds showed marked improvement and were classified as Grade 1. An electrocardiogram was also improved and was reported as normal. At that time the patient weighed 300 pounds.

Case 13. A 37-year-old gravida I had first been seen at the age of 33 when she was single. Because of weight loss and easy fatigability she had consulted a physician, who had found hypertension and referred her to the hospital for study in May, 1941. The blood pressure on admission was 210/150, with an average of 195/110 when the patient was resting in bed. The heart shadow was within normal limits. An electrocardiogram showed normal rhythm, inverted T waves in Lead 3 and a normal Lead 4. The eye grounds showed slight tortuosity and arteriovenous nicking. Pyelograms disclosed good excretion of the dye through both kidneys within 5 minutes. The urine concentrated to 1.018 and contained no albumin, and the sediment was normal. A phenolsulfonephthalein test showed 35 per cent excretion of the dye in 20 minutes and 45 per cent in 1 hour. On sedation the blood pressure fell to 180/110. The patient was discharged with the diagnosis of essential hypertension.

In November, 1942, she was readmitted for splanchnicectomy. The laboratory data were essentially the same as those on the previous admission. A urea clearance showed a maximum excretion of 60 per cent with a volume of 145 cc. and of 68 per cent with a volume of 280 cc.

On December 1 a left lumbodorsal splanchnicectomy was performed, with excision of the sympathetic trunk from the tenth dorsal to the second lumbar segment, inclusive. On December 13 an identical operation was performed on the right side. On both sides the great splanchnic nerves were removed from the semilunar ganglions to above the midthoracic level. Biopsies taken from both kidneys revealed early renal arteriolar medial hyperplasia. After an uneventful convalescence the patient was discharged on January 11, 1943, with a blood pressure of 140/80.

The patient married in 1943 and became pregnant in December, 1944. The pregnancy was entirely normal. The highest blood pressure recorded was 138/85. The urine was consistently free of albumin, and the total weight gain was 18 pounds. She was delivered on October 9, 1945, of a living female infant and was discharged on the 14th post-partum day with a blood pressure of 132/90. Six weeks after delivery the blood pressure was 128/90.

Case 14. A 39-year-old gravida V was admitted in January, 1943, complaining of headache and vertigo. She had developed hypertension during the first pregnancy 10 years previously. The hypertension had become progressively severer with three subsequent pregnancies.

Physical examination revealed an obese woman weighing 200 pounds. The blood pressure was 180/130, the range during postural and cold tests being from 170/106 to 218/132. The heart was not enlarged, but the aorta was tortuous. An electrocardiogram was normal. The urine showed a + test for albumin and a maximum concentration of 1.020. The sediment was normal. The nonprotein nitrogen was 30 mg. and the uric acid 2.9 mg. per 100 cc., and the phenolsulfonephthalein test showed 30 per cent excretion of the dye in 15 minutes and 90 per cent in 2 hours. Intravenous pyelograms were normal. On sedation the blood pressure fell to 130/78.

On January 21 a right lumbodorsal splanchnicectomy was performed, the sympathetic trunk being removed from the ninth dorsal to the second lumbar segment, inclusive. On February 3 a similar operation was performed on the left, the sympathetic trunk being removed from the eighth dorsal to the second lumbar, inclusive. The great splanchnic nerves were removed on both sides from the celiac ganglions to the midthoracic level. Biopsies taken at operation were reported as showing a Grade II chronic vascular nephritis. The patient was discharged on February 24, with a blood pressure of 185/105.

The patient conceived in December and experienced an uncomfortable pregnancy during which she gained 56 pounds. The blood pressure ranged between 130/70 and 150/90. The urine remained free from albumin. She was delivered on August 29, 1944, of a full-term, living infant. The blood pressure was 129/78, and the urine was normal when the patient was seen 18 months post partum.

Moderate to severe hypertension had been present in all cases until the patients had been treated by splanchnicectomy. Fourteen living infants were delivered, the oldest of which is now four years of age. One baby was stillborn, owing to premature separation of the placenta.

Three of the patients had so-called "malignant hypertension" prior to lumbodorsal splanchnicectomy. They responded favorably to operation and tolerated subsequent pregnancy well. Both mothers are living and well, having exceeded the average life expectancy for patients with malignant hypertension, and having living children. This experience is regarded as unique. In 1 case the pregnancy was completely uneventful, and in the other a transient rise in blood pressure associated with the occurrence of a + test for albumin necessitated delivery a few days prior to full term. In the third case the pregnancy was uneventful, but the puerperium was complicated by a psychosis.

The other 11 patients had severe essential hypertension, with or without chronic pyelonephritis. These patients are also living and well following pregnancy. The hypertension is much improved over that prior to splanchnicectomy. There is as yet no definite evidence that pregnancy has materially affected the postoperative course of the hypertensive process in these cases. In 5 cases increasing hypertension associated with increasing albuminuria occurred during the third trimester, necessitating delivery prior to full term. In no case did the hypertension increase prior to the seventh month of pregnancy.

It should be emphasized that in these cases, as in patients who have not had a previous lumbodorsal splanchnicectomy, one should not procrastinate when the signs of toxemia appear. The established and accepted criteria for termination of pregnancy should be closely observed.

It seems most unlikely that the majority of these patients could have obtained living children without suffering material cardiovascular damage or an increase in the severity of the hypertension following pregnancy had not lumbodorsal splanchnicec-

tomy been performed. In 1 case the operation was performed during the first trimester; so far as we know this is the first case on record treated in this manner. In the other cases the interval between operation and pregnancy ranged from three to ninety-six months, the average being thirty months.

Conclusions

It is known that lumbodorsal splanchnicectomy is a useful therapeutic measure in the treatment of hypertension and hypertensive cardiovascular disease.

Following a satisfactory response to operation, pregnancy, if carefully supervised, appears to be safe and permissible.

The experiences presented above lead us to believe that following this operation certain hypertensive women may be able to tolerate pregnancy, which would otherwise be impossible or extremely hazardous. This is particularly true in the younger age group with severe essential and even malignant hypertension.

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DISTURBANCES OF METABOLISM ASSOCIATED WITH HEAD INJURIES*

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Diabetes is a wonderful affection, not very frequent among men, being a melting down of the flesh and limbs into urine. Its cause is of a cold and humid nature as in dropsy. The course is the common one, namely the kidneys and bladder; for the patients never stop making water, but the flow is incessant, as if from the opening of aqueducts. The nature of the disease, then, is chronic, and it takes a long period to form; but the patient is short-lived, if the constitution of the disease be completely established; for the melting is rapid, the death speedy. Moreover life is disgusting and painful; thirst, unquenchable; excessive drinking, which however, is disproportionate to the large quantity of urine, for more urine is passed; and one cannot stop them either from drinking or making water. Or if for a time they abstain from drinking, their mouth becomes parched and their body dry; the viscera seem as if scorched up; they are affected with nausea, restlessness, and a burning thirst; and at no distant time they expire. Thirst, as if scorched up with fire. But by what method could they be restrained from making water? Or how can shame become more potent than pain? and even if they were to restrain themselves for a short time, they become swelled in the loins, scrotum, and hips; and when they give vent, they discharge the collected urine, and the swellings subside, for the overflow passes to the bladder. . . . Hence the disease appears to me to have got the name diabetes, as if from the Greek word διαβητης (which signifies a siphon), because the fluid does not remain in the body, but uses the man's body as a ladder (διαβαθρη)‡ whereby to leave it. . . . The cause of it may be that some of the acute diseases may have terminated in this; and during the crisis of the disease may have left some malignity lurking in the part. It is not improbable also, that something pernicious, derived from the other diseases which attack the bladder and kidneys, may sometimes prove the cause of this affection.

THIS vivid description was written by Areteaus, the Cappodocian,[1] who lived around 200 A.D. and whose careful accounts of pathologic conditions rank next to those of Hippocrates. It is interesting to note that this picture includes features of diabetes insipidus, diabetes mellitus and nephritis; this confusion persisted for many years. In the seventh century the Brahmin physician Susruta recognized the "honey urine," and four hundred years later Avicenna noted the sweet taste of the urine. It was not until the seventeenth century, however, that Thomas Willis made a clear distinction between diabetes mellitus and diabetes insipidus, followed in a few years by Johann Brunner's early experimental proof of the relation of the pancreas to diabetes mellitus. The relation of the brain to these processes was indicated by Claude Bernard's puncture of the fourth ventricle with resultant glycosuria in 1849. Bramwell,[3] in 1888, stated as follows:

> Tumours of the pituitary body are in many instances attended with an excessive development of the subcutaneous fat, and in some cases with the presence of sugar in the urine or with simple polyuria (diabetes insipidus). Whether these symptoms are due to the fact that the pituitary body is itself diseased, or whether, as seems more likely, to the secondary results which tumours in this situation produce in the surrounding cerebral tissue, has not yet been decided.

These investigators were apparently well ahead of their times, for it was not until early in the present

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‡This Greek word might be better translated literally "something to step through." The Latin translation is "quia humor in corpore non remanet, sed homine, tanquam canali quodam, ad effluendum utitur"[2] — that is, "because the fluid does not remain in the body but uses the man as a sort of water pipe for flowing off."

century, when Cushing and his pupils made their far-reaching studies of the hypophysis and its neighborhood, that the notion of metabolic control by brain centers gained any real acceptance. The present-day concept of this influence of the central nervous system is given by Ranson[4] as follows:

> Resting on the optic tract lateral to the chiasm is a compact group of rather large cells, the supra-optic nucleus. Fibres arising in this nucleus along with some other fibres of hypothalamic origin run along the infundibulum to the posterior lobe of the hypophysis. Through this hypothalamico-hypophyseal tract the hypothalamus is in position to influence the functions of the hypophysis. One or the other of these two structures, or both together, exert an important control over the utilization of sugar, fat and water in the body.

To this Wiggers[5] adds:

> The structures of the hypothalamus are head centers for the sympathetic nervous system. Stimulation or lesions in this region may cause alterations in heart rate and blood pressure, sweat secretion, carbohydrate protein and fat metabolism, temperature regulation, evacuation of bladder and rectum, polyuria, dilatation of the pupils, widening of the palpebral fissures and bulging of the eyeballs.

Changes in body metabolism due to tumors involving this region are well recognized. Disorders following encephalitis of this area of the brain are not uncommon; comparable changes following trauma, however, are much less frequent, and it is with these disturbances of metabolism associated with head injuries that the present paper is concerned.

That such changes do occur has been noted by several writers. Bailey,[6] in 1906, reported the appearance of transient glycosuria, lasting from twenty-four hours to five or six days, in patients with head injuries. This was found with fractures of the vault or of the base, and in some patients with no known fracture. In some cases the glycosuria was accompanied by an increase in the amount of urine, and in others polyuria existed without sugar. In 1940 Gross and Ehrlich[7] mentioned glycosuria due to hypothalamic damage and stated that diabetes insipidus might arise from the same cause.[8] Such injury was considered likelier to occur in the presence of fractures of the middle cranial fossa. Rowbotham,[9] in 1942, gave the following interesting description:

> Traumatic diabetes insipidus usually declares itself early in convalescence though it may not appear till several months after the injury. The outstanding symptom in this condition is insatiable thirst with a desire for water to assuage it. In severe cases a patient will drink 1 or 2 pints of water at a time and has to take copious supplies to bed with him as he so often wakens in the night and wants to drink. Fluids taken by mouth are rapidly excreted by the kidneys so that a patient tends to lose weight rather than to become waterlogged. Severe headaches, loss of physical energy, and mental depression are commonly associated with the symptoms of thirst. One young patient of mine who had been severely concussed and whose skull had been fractured through the pituitary fossa needed at least 12 pints of fluid in the day to satisfy his thirst, and once drank as many as 15 pints. The amount of water he passed was graphically described by his mother as being worthy of a donkey. In fact a large bucket was left under the bed for his use as his nocturnal perigrinations used to disturb the whole household. This disturbance of water metabolism was readily controlled by hypodermic injections of 0.5 cc. of pituitrin night and morning. In six months after the injury this young man made a complete recovery. The tendency in all cases of traumatic diabetes insipidus is toward spontaneous cure. It is useless to restrict the amounts of fluids taken in an attempt to control the diabetes, because this only leads to dehydration and toxemia. Usually injections of pituitrin will keep a patient's thirst under reasonable control until spontaneous cure of the diabetes results. Severe and persistent cases may necessitate a total thyroidectomy as suggested by the work of Mahoney and Sheehan.

All these are cases of disturbed use of sugar and water in the body. The only example of upset fat metabolism of which I have found a report thus far is also given by Rowbotham[10]:

> A pathological increase in weight due to excessive deposits of fat occasionally results from a basal injury, as evidenced by the case of a late Professor of Surgery in Manchester who fell from a horse and fractured the base of his skull. Following the injury, he became extremely stout, and this stoutness was associated with very definite dispositional changes.

The small number of reports of actual patients suffering from these disorders indicates either a lack of interest in these conditions or a considerable rarity of occurrence. My interest was aroused by the onset of severe diabetes insipidus in one patient and of an unusual disturbance of fat metabolism in another; in both, the findings were so striking that they demanded attention, stimulating a search for similar disorders in other patients. In the treatment of over 2500 patients with head injuries in the past ten years 7 cases of metabolic disturbance, 2 of sugar metabolism, 4 of water metabolism and 1 of fat metabolism have been noted; none involving protein metabolism have been recognized. It is not at all unlikely that many minor disorders have been overlooked, since interest was only recently directed to this subject. A careful study of these factors in all patients is now being made, in the hope that a reasonably accurate estimate of their incidence will be possible.

Sugar Metabolism

Only 1 case of transient glycosuria similar to that reported by Bailey[6] has been observed. This occurred in a patient who later developed diabetes insipidus and whose record is more fully discussed in the consideration of water metabolism. Since many of the patients were given glucose by vein soon after the injury, some minor disturbances may well have been concealed. Another case of upset sugar metabolism was the following:

> A 27-year-old man was admitted to the hospital on April 28, 1945, following an automobile accident in which he was said to have struck his head on some part of the car. On admission he was in severe traumatic shock and was in coma, with evidence of serious generalized brain damage but without clinical signs of skull fracture. It was learned that he was mildly diabetic and had been taking 20 units of protamine insulin daily. In view of this, the control of the diabetes was kept in mind from the start, and the Medical Service took over that part of the problem. There was no indication that the coma was in any way due to diabetes — the urine showed a +++ test for sugar and no acetone, and the blood

glucose was 175 mg. per 100 cc. The patient was given a carefully regulated diet by two feedings a day with a stomach tube, the urine and blood sugar were followed and insulin was given as indicated. He developed a bilateral Babinski response, slightly more marked on the right than on the left, and there was apparently somewhat more power in the movements of the left arm and leg than in the right. Fundus examination showed the disks to be sharply outlined, with good physiologic cupping, questionable minimal pallor of the arteries and many small round hemorrhages deep in the nerve-cell layer of the retina around the central area, especially on the left side. The presence of an acute subdural hematoma was suspected, but the evidence was not considered sufficient to warrant exploration. On the 3rd day the patient began to show some response to stimuli, and on the 4th day he answered questions and recognized members of his family. On the 5th day, in spite of the most careful attempts at control, the blood glucose rose suddenly to 536 mg. per 100 cc., and signs of diabetic coma developed. This proved to be resistant to treatment, and for the next 3 days the control of the diabetes was a serious problem. The signs of brain damage then subsided, and the diabetes returned to a mild, easily controlled condition. X-ray examination showed no signs of skull fracture. The patient made a good recovery and was discharged on the 42nd day.

He has subsequently been followed at rather infrequent intervals, since he does not take his condition seriously and gets along quite well on a rather haphazard dietary regime with occasional small doses of insulin. He shows no organic residual signs of the brain damage.

In this connection, it is worthy of note that Cushing,[11] in his Lister Memorial Lecture in 1930, stated, "The diabetes mellitus of acromegaly, moreover, proves to be notably resistant to treatment by insulin and it has been repeatedly shown that posterior-lobe extract (pituitrin) will diminish or wholly counteract the blood-sugar-reducing effect of this product." It seems reasonable to suppose, then, that in the case presented above the marked temporary resistance of the diabetes to previously effective insulin was related to injury of the general area of the brain under discussion.

Water Metabolism

The following cases of disturbance of water metabolism were associated with trauma:

A 26-year-old shipyard worker fell about 15 feet from a scaffold, landed on his feet without striking his head and was rendered unconscious for about ½ hour. He was then dizzy and nauseated, complained of sharp pain in the frontal and occipital regions, and had no memory of the events concerned in the accident or for several hours thereafter. He had some blurring of vision associated with weakness of convergence of the eyes, but neurologic examination was otherwise normal. X-ray films of the skull and of the entire spine showed no evidence of injury, and there were no clinical signs of fracture. Lumbar puncture showed normal pressures, a moderate number of red cells and some elevation of the spinal-fluid protein. There was no urinary disturbance while the patient was in the hospital. He apparently made a good recovery and was discharged on the 21st day.

Ten days later, when he reported for examination, he said that he felt tired and depressed, that he was passing large amounts of urine frequently and that for this reason he had to get up many times at night. Examination of the urine showed almost colorless fluid with a specific gravity of 1.002 and no sugar. Further x-ray films of the region of the sella turcica were taken but showed no deformity or evidence of fracture. Neurologic examination gave no abnormal findings, and there were no signs of any field defect. Attempts to obtain a record of fluid intake and output were unsuccessful. The condition cleared slowly and steadily without treatment, and in 4 months the urine was normal in amount and concentration. The patient has subsequently remained free of symptoms.

A 22-year-old woman was admitted to the hospital on August 26, 1945, after having been knocked down by a hit-and-run driver. She was in deep traumatic shock and had a compound basal skull fracture with blood in the nose and pharynx and with a mixture of blood and cerebrospinal fluid draining from the right ear. She also had a compound fracture of the left leg, a fracture of the right ankle, fractures of the left lower ribs and a contusion of the left kidney. She was semicomatose. The pupils were moderately dilated; the right pupil reacted normally to light, whereas the left showed a curious summation response — that is, continuous stimulation with light produced no effect, but repeated flashes of light caused contraction. There were no other definitely abnormal neurologic findings. The patient was given large amounts of plasma and some physiologic saline solution by vein; the shock was gradually overcome, and the fractures were treated. She regained consciousness in about 3 days, but was disoriented, noisy and unco-operative and did not become clear and rational for about 4 weeks. The summation response disappeared within 2 days. After a week she developed a left internal strabismus, which cleared up gradually in the course of several weeks. When it became possible to test the visual fields, no abnormality was apparent.

Examination of the urine on the day of admission, and before any glucose had been given, showed a specific gravity of 1.010, a +++ test for protein and a ++ test for sugar, no acetone and many red cells. The blood glucose at that time was within normal limits. The sugar disappeared permanently within 2 days, and the red cells and protein cleared rapidly as the injury to the kidney healed. The specific gravity of the urine fell steadily, thirst and water intake increased, and the amount of urine passed became greater. By the 12th day after the accident, the patient presented a fully developed picture of traumatic diabetes insipidus, the intake being 5620 cc. and the output 6000 cc. This excessive water exchange continued for about a month, the highest intake recorded being 11,303 cc. and the maximum output being 10,000 cc. Frequently, the amount of urine passed was greater than that of the fluids taken in. The specific gravity of the urine varied from 1.001 to 1.004. Urea nitrogen, glucose, cholesterin and sodium chloride levels in the blood were normal throughout the course of the disease. Sodium chloride excretion in the urine was reduced to 30 mg. a day at the start, and rose slowly as the condition progressed. The levels of calcium and phosphorus in the blood were unaffected.

Treatment by injection of posterior pituitary extract gave fleeting and rather inconstant relief of symptoms; the use of Pitressin Tannate in Oil gave somewhat better results, but there was no marked improvement until about 5 weeks from the onset of the trouble. At the end of 7 weeks, with the use of the latter, the intake and output were essentially normal. Treatment was then stopped, and there was a prompt rise to an average intake of 3000 cc., with an average output of 2500 cc. In the course of the next 4 weeks, without further treatment, the symptoms gradually subsided and at the end of that time there was a normal exchange of fluids.

The progress of the patient has subsequently been followed, and there has been no recurrence of any trouble. Treatment seemed to have controlled the symptoms rather inadequately but to have had no real effect on the course of the disorder.

The third patient was a 50-year-old man who had relatively mild brain congestion following a fall, with no evidence of skull fracture. He developed unusual thirst, polyuria and a urine of low specific gravity about 3 weeks after the injury. This condition cleared up spontaneously in another 3 weeks.

The fourth patient was a 53-year-old textile worker who was struck on the head by the flying end of a broken belt in April, 1943. Following this he developed severe headaches and increasing weakness of the right arm and leg, with slurring speech, auditory hallucinations and personality changes of a moody and combative nature. In January, 1944, a right fluid subdural hematoma was drained, and later exploration for a left subdural hematoma proved negative. Since that time the patient has shown a considerable but slow improvement, and he still has some confusion and dizziness. In July, 1946, more than 3 years after the injury, the appetite increased markedly, so that he ate a dozen eggs at a time, but there was no weight increase. There were no clinical signs

of thyroid overactivity, but the basal metabolic rate was +24 per cent. This excess appetite has decreased, but 4 weeks ago he began to drink large amounts of water and other fluids, which failed to satisfy his thirst, and passed large quantities of urine. According to home records, whose accuracy may be open to some question, the intake was from 5000 to 6000 cc., and the output 7000 to 8000 cc. Examination of the urine showed a specific gravity of 1.001, with no albumin or sugar and with no abnormal elements in the sediment. Examination of the blood showed normal values for urea nitrogen and sugar, with that for cholesterol slightly elevated to 252 mg. per 100 cc. The patient has been treated with injections of Pituitrin, and a week ago the intake and output were approximately 2000 cc. each, and the specific gravity of the urine was 1.010. It seems not unlikely that he has metabolic disorders involving more than the use of water, and he is being studied with this possibility in mind.

Fat Metabolism

The single case of disturbed fat metabolism after head injury was as follows:

In February, 1945, a 47-year-old shipyard foreman entered the hospital about two weeks after a fall in which he had struck the back of the head. There had been a short period of unconsciousness, followed by severe occipital headache and two episodes of vomiting. He then became lethargic and felt weak, was unable to concentrate and had partial amnesia for recent and remote events. Prior to the accident he had had charge of the work on three different ways at the yard, his duties involving constant climbing and physical activity, and he had lost no time from work. He had worked many hours overtime and felt somewhat tired, but his superiors considered his work excellent.

Physical examination showed a healed laceration, about 3 cm. long, in the occipital region. The right pupil was slightly smaller than the left; both reacted sluggishly to light, the left a little more slowly than the right. The optic disks were normal; there was slight weakness of the right masseter muscle and of the right facial muscles; the superficial reflexes were diminished on the right, and the deep reflexes were diminished on the left. X-ray films of the skull, including particular examination of the sella, showed no fracture. Lumbar-puncture findings were within normal limits.

It was at first thought that the patient might have a subdural hematoma, but the symptoms improved so much on bed rest that exploration was considered inadvisable. In the course of a routine examination of the blood he was found to have a grossly visible lipemia, and studies to determine its cause were begun. The urine was normal except for a slight trace of protein and a few granular hyaline casts. Examination of the blood showed normal red-cell and white-cell counts and differential distribution and a normal amount of hemoglobin; the urea nitrogen, total protein and glucose levels were normal. The total fat in the blood was 3 per cent (normal, 0.5 to 0.7 per cent). The cholesterol was 584 mg. per 100 cc. (high normal, 220 mg.). The total blood lipid was 4.4 per cent, and the lipid phosphorus was 21.5 mg. per 100 cc. The prothrombin time and icteric index were normal, and a glucose-tolerance test was also normal. A hippuric acid test was 143 per cent of normal. There was no evidence of xanthomatosis.

On repeated examinations the lipemia persisted, and the cholesterol stayed at about the same level. After careful consideration, the Medical Service concluded that the patient had a lipemia of unknown origin. A well known authority on fat metabolism saw the patient and could give no explanation for the lipemia other than the trauma; he believed that if the disturbance in the use of fat disappeared as the head injury cleared it would confirm the impression that the condition was due to brain damage. The neurologic signs subsided slowly, and the patient was discharged at the end of 1 month complaining of occasional headaches, irritability, depression, muscular weakness and easy fatigability.

His condition has been followed since that time by clinical examinations and cholesterol determinations. In April, 1946, the cholesterol was 680 mg. per 100 cc.; in May it was 432 mg., and in July it was 496 mg. At that time the patient was put on a diet low in cholesterol, and by October the cholesterol had dropped to 284 mg. per 100 cc.; he was much less irritable and was able to undertake some physical activity without marked fatigue. Eleven months after the accident the cholesterol was 176 mg. per 100 cc., and the patient felt much better. With the withdrawal of most of the dietary restrictions the cholesterol rose to a little above normal levels, but it has now leveled off. The patient's strength is returning, his disposition is good and he is able to work.

In this case, as in diabetes insipidus, it seems likely that treatment served to relieve symptoms by lowering the amount of cholesterol in the blood without actually affecting the course of the disease.

Summary

Seven cases of metabolic disturbance associated with head injuries are presented for consideration. There is, of course, no real proof that any one of these examples of abnormal metabolism was actually due to a traumatic lesion of the hypothalamic region; no study was made prior to the injury, there was no death, and tissue examination was not possible. The patients represented a group of supposedly normal people who suffered head injuries involving slight to severe brain damage, who then, at periods varying from a few hours to three years later, developed disturbances in the use of sugar, water and fat such as those known to occur when the hypothalamus is injured, and whose disorders cleared up as the head injury healed. It thus seems reasonable to suppose that brain damage was a causal factor. A realization of the possible occurrence of such upsets, and a continued search for them will, in all probability, result in more frequent recognition and a better understanding of these interesting disturbances of metabolism.

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Discussion

Dr. Donald Munro (Boston): This excellent and well documented paper deserves more than passing notice. The subject is extremely important and so far as I know, nothing so thorough as this has previously been published.

The problem of the initiation of diabetes mellitus by trauma to the head is brought up from time to time before compensation boards in various states, and I happen to have been involved in such a discussion. On a search for authoritative statements regarding whether or not trauma to the head actually caused diabetes mellitus, it was impossible to find any really substantive statements. Now we have an authority that we can quote.

In connection with this experience, I called Dr. Elliott P. Joslin to find out whether he had any knowledge about the causal relation between head injury and diabetes mellitus. He stated that, so far as he knew, there is no such relation. In my experience, I have not knowingly seen a patient who has sustained a head injury and who, as a result of that injury, has had diabetes mellitus. The combination is not frequent.

Diabetes insipidus, of course, is a different story, although a relatively rare disease; it is, again, extremely useful to have these cases on record, particularly when they have been worked up so carefully.

AN OUTBREAK OF INFLUENZA B INFECTION*

Epidemiologic Observations

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ALTHOUGH much knowledge concerning the epidemiology of influenza has been acquired over the years, more specific information has awaited the isolation of the etiologic agents. The discovery of the influenza B virus in 1940 simultaneously by Francis[1] and Magill[2] greatly facilitated the researches on the epidemiology of this disease. Nevertheless, data concerning the transmission of influenza B have not accumulated at a rapid rate. In some outbreaks it has been difficult or impossible to isolate the influenza B virus, and identification of cases in such circumstances necessarily depended on serologic studies. Furthermore, in extensive epidemics, it is not often practical to obtain acute and convalescent blood specimens from more than small samples of the population being investigated.

It has been shown that influenza B infection occurs as both an endemic and an epidemic disease. In Argentina, for example, sporadic cases of influenza B infection appeared in 1941 over a period of several months (June to October). This was in contrast to a sharp outbreak of influenza A infection during the previous year.[3] Beveridge and Williams[4] noted the sporadic occurrence of influenza B infection in Australia from June to September, 1943. Hare et al.[5] reported a high incidence of upper respiratory infection in various localities in Canada. Serologic evidence indicated that 23 per cent of the cases were due to influenza B virus. Localized outbreaks, on the other hand, have been reported from a convalescent home[1] and from a hospital for mental diseases.[6] In the latter institution 71 patients out of 1440 developed influenza B infection. In one unit the combined incidence of clinical and subclinical influenza was 20 per cent.

Influenza B may occur either alone or in association with influenza A. Lennette et al.,[7] in a study of twelve outbreaks of influenza, found cases of influenza A infection in all but two epidemics, whereas cases of influenza B infection were encountered in only five epidemics. Influenza of unknown etiology occurred in each epidemic and accounted for 11 to 80 per cent of all the cases.

There is some statistical evidence that widespread epidemics of influenza B infection have occurred at intervals of four to six years.[8] Francis[9] suggested a four-year cycle on the basis of two known widespread epidemics of influenza B infection in 1936 and 1940.

Beginning in mid-April, 1945, small outbreaks of influenza B infection were reported from many areas in and outside the United States and were identified serologically or by virus isolation.[10] Late in November and in December of that year an increased incidence of clinical influenza was noted in several communities in the Greater Boston area. Although the infection was generally prevalent throughout the entire area, there was considerable variation in incidence from one community to another.

Purpose and Methods

During the second week of December, 1945, our attention was called to reports indicating that influenza had assumed epidemic proportions in the schools of Needham, Massachusetts. In the junior high school, with an enrollment of 577 children, 50 per cent absenteeism had occurred. In the absence of detailed information in the literature concerning the transmission of influenza B infection in schools,

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a study of this aspect of the epidemiology was instituted. Although influenza was prevalent throughout all schools in Needham, the study reported in this paper was limited to the high school, the junior high school and one of the elementary schools (Avery School).

With the co-operation of the local school and health-department nurses, visits were made between December 13 and 16 to the junior high school and to the homes of some of the pupils who were absent because of symptoms of influenza. At that time detailed histories were obtained, physical examinations were done on a number of the pupils who were acutely ill and blood was drawn for serologic studies. Throat garglings were also obtained from a few patients who were acutely ill with typical symptoms of clinical influenza and with temperatures of 101°F. or higher. Histories concerning recent illness and blood for serologic studies were also obtained from as many household contacts as possible. A second visit was made to each of the same homes between December 29 and January 2, when second samples of blood were drawn and individual histories taken from the patients and the household contacts.

Epidemiologic data concerning illnesses and absenteeism during the period of the epidemic were obtained by means of a questionnaire given to each student in the three schools chosen for the study. Again, the school and local health-department nurses participated by explaining to teachers, parents and pupils the purpose of the investigation and by distributing and collecting the questionnaires. The school records were also examined for detailed information concerning absenteeism.

In an attempt to differentiate cases of common cold and other illness not related to influenza, specific information was sought in the questionnaire concerning such symptoms as malaise, headache, cough, coryza, sore throat, pain in the eyeballs, back and extremities, vomiting and diarrhea. There were other questions regarding date of onset, duration of symptoms, the presence or absence of fever and the total duration and degree of temperature rise. Patients presenting a majority of the symptoms mentioned above, in addition to a fever of at least twenty-four hours' duration, were tabulated as cases of influenza. Fortunately, the clinical picture was quite definite; the onset was sudden, prostration marked and in at least half the cases studied the duration of illness was four days or longer. The incidence of the common cold was low in this community during the time of the epidemic.

Laboratory Studies

The methods used in the laboratory investigations and the results obtained are presented in detail elsewhere.[11] Attempts to isolate viruses from the throat washings of the patients from Needham were unsuccessful at first. Two strains of virus, however, were readily established in other cases that were studied at that time, and a third strain was subsequently isolated in one of the Needham cases. These epidemic strains were identified as influenza B and were used for the serologic studies along with the PR8 strain of influenza A virus and the Lee strain of influenza B virus. Tests for inhibition of chicken erythrocyte agglutination and complement-fixation tests were done on serums taken from patients during the acute and convalescent phases and on those obtained at the same time from the household contacts. The results of the serologic tests are summarized in Table 1.

Table 1. *Results of Tests for Influenza Antibodies in Cases and Household Contacts.*

Subjects	No. Tested	No. Showing Significant Rise in Antibody Titers			
		Influenza A		Influenza B	
		PR8 strain		*Lee strain*	*epidemic strains*
Patients with clinical influenza. ..	19	0		13*	16
Household contacts.....	20	0		0	0
With symptoms of common cold	4	0	0	0	
With gastrointestinal symptoms	4	0	0	0	
Without illness	12	0	0	0	

*An additional case showed a rise by complement fixation but not by inhibition of agglutination.

Of the 19 typical cases of clinical influenza included in this study 16 yielded convincing evidence of infection with influenza B virus by significant, and in most cases marked, rises in the titers of antibodies for the Lee strain and for the epidemic strains but not for the PR8 strain. The 3 cases in which no rise in antibodies was demonstrated for any of the viruses used were all in members of the same family, and these were the only persons studied in that household.

All the household contacts who did not have symptoms of clinical influenza failed to show a significant — that is, a fourfold — rise in titer of antibodies for either the PR8 strain of influenza A virus or the Lee strain of influenza B virus. The serums of these persons were also tested with the epidemic strains, and no significant rise in titer of antibodies for any of them was demonstrated. Included among the contacts were 4 subjects who had coryza without fever or systemic symptoms and were regarded as having the common cold, 4 others who had low-grade fever and gastrointestinal symptoms, mostly diarrhea, and 12 healthy persons who had had no recent illness. Only 2 of the contacts were school children; the others were adults — most of them parents of the patients with influenza.

Epidemiology

During the interval December 2–21 a total of 484 cases of influenzalike infection occurred in the three schools included in the study. The attack rate was highest — 53.7 per cent — in the junior high school, and lowest — 24.4 per cent — in the senior high

school, the difference being significant statistically. The standard deviation of the difference between these rates is 29.3 ± 2.8. The difference in the rates between the junior high and Avery schools, however, was not found to be statistically significant. The

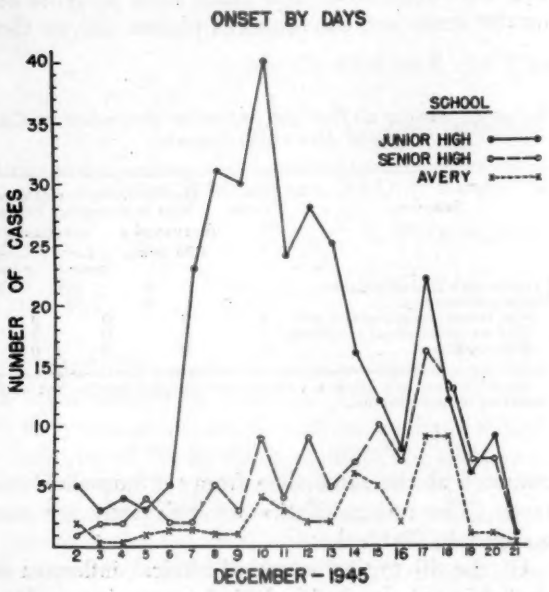

FIGURE 1. *Distribution of Cases in All Schools according to Date of Onset.*

standard deviation of the difference between the latter rates is 9.2 ± 5.0 (Table 2).

The distribution of cases in the three schools according to the date of onset is presented in Figure 1.

TABLE 2. *Attack Rates in Three Schools.*

SCHOOL	SCHOOL POPULATION	NO. OF CASES	ATTACK RATE
			%
Senior High	492	120	24.4 ± 1.94
Junior High	577	310	53.7 ± 2.08
Avery	122	54	44.7 ± 4.50
Totals	1191	484	
Average			40.6 ± 1.42

The day of highest incidence in the junior high school preceded that in the senior high and Avery schools by a week. A second peak occurred in the junior high school at the time of highest incidence in the other two. All peaks occurred at or just after a week end. A sharp epidemic curve was noted in all three schools.

The peak in the seventh, eighth and ninth grades of the junior high school occurred within a period of forty-eight hours (Fig. 2), indicating widespread dissemination of infection through all three grades at about the same time. Of 120 cases in the eighth grade 81, or 67 per cent, appeared in the seven-day period from December 7 to 13. In the ninth grade 64 of 109 patients, or 59 per cent, became ill during the same week. Although there was considerable variation in the curve for each grade, it is apparent that a fairly well defined rise and fall occurred in each group.

The attack rates in individual classrooms varied from 38.5 to 82.9 per cent. Out of seventeen classrooms in the junior high school, the attack rate was

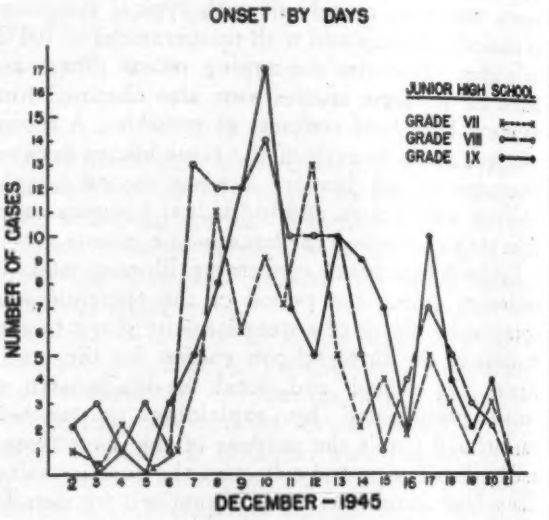

FIGURE 2. *Distribution of Cases in the Junior High School according to Date of Onset.*

50 per cent or higher in nine and less than 40 per cent in three (Table 3). The attack rate for the entire school was 53.7 per cent, 310 children out of the total of 577 enrolled having developed clinical influenza from December 2 to 21.

Total absenteeism as compared with that caused by influenza is demonstrated in Table 4. In the junior high school at the height of the epidemic a major proportion of children absent from school were ill with influenza. On December 10, for example, 123 (78.3 per cent) of 157 absentees were ill with influenza and only 34 pupils (approximately 6 per cent) of the total enrolled were absent for causes other than influenza.

In the senior high school, where the attack rate was lower, the proportion of children absent because of influenza was considerably less than that in the junior high school. From December 10 to 18, at the very height of the epidemic, the percentage of absenteeism due to influenza varied from 14.8 to 54.5.

In the Avery School the bulk of absenteeism was due to causes other than influenza. On several occa-

sions during the peak of the epidemic less than a third of the children out of school were absent because of influenza.

In all three schools the proportion of total absenteeism due to influenza increased as the epidemic progressed. On December 4 the percentages for the Avery School and the senior high and junior high schools were 4.0, 10.7 and 37.5 respectively, and ten days later they had risen to 31.0, 37.4 and 73.0 in the same order. In general the figures for percentage absenteeism due to influenza were high in the junior high school, low in the Avery School and intermediate in the high school. No other contagious disease was prevalent in the three schools during the period of the study. Hysteria on the part of parents who did not permit their children to attend school lest they be exposed to the infection was responsible for a large proportion of absenteeism due to causes other than influenza.

Discussion

It has been stated that the virus of influenza B spreads less rapidly than that of most A strains and that ordinarily it does not produce extensive outbreaks.[12] The high incidence of this infection in the Needham schools is evidence that it may at times resemble influenza A virus in its rate of transmission. Well defined epidemic curves were noted in the three schools selected for the study and also in the individual grades of the junior high school. High attack rates prevailed in individual classrooms and throughout the school system.

The incidence of infection in the junior high and Avery schools was significantly higher than that in the senior high school. Both the senior and junior high schools were attended by pupils living throughout the entire community, and since cases were reported from every homeroom and grade in both schools, it is apparent that opportunity for exposure to infection was present in each. It may therefore be postulated that the variation in age distribution was the prime factor in the difference between rates in the senior high school on the one hand and those in the junior high and Avery schools on the other.

The high attack rates observed in the Needham schools have particular significance when consideration is given to the choice of groups best suited for vaccination against influenza. It is apparent that in a susceptible population, large numbers of children will develop influenza B infection following adequate exposure and that an effective immunizing agent would be of value in diminishing school absenteeism.

Table 3. *Attack Rates by Classroom and Grade (Junior High School).*

Grade	Room No.	No. of Pupils	No. Ill	Attack Rate
				%
Seventh	1	26	10	38.5
	3	30	13	43.3
	5	26	10	38.5
	201	28	15	53.6
	204	28	21	75.0
	302	29	12	41.4
Totals		167	81	
Average				48.5
Eighth	202	34	14	41.2
	209	38	26	68.4
	304	36	14	38.9
	306	33	22	66.7
	310	35	15	42.9
	312	35	29	82.9
Totals		211	120	
Average				56.9
Ninth	207	39	23	59.0
	301	38	19	50.0
	307	41	22	53.7
	308	45	20	44.4
	309	36	25	69.4
Totals		199	109	
Average				54.7
Grand totals		577	310	
Grand average				53.7

Table 4. *Absenteeism during Influenza Outbreak.*

Date	Avery School*		Senior High School†		Junior High School‡	
	Total pupils absent	Pupils with influenza	Total pupils absent	Pupils with influenza	Total pupils absent	Pupils with influenza
December, 1945						
3	31	1 (3.2%)	20	2 (10.0%)	25	5 (20.0%)
4	25	1 (4.0%)	28	3 (10.7%)	24	9 (37.5%)
5	26	2 (7.7%)	31	5 (16.1%)	25	8 (32.0%)
6	42	4 (9.5%)	36	7 (19.4%)	30	13 (43.3%)
7	63	5 (7.9%)	52	6 (11.5%)	50	27 (54.0%)
10	31	8 (25.8%)	54	8 (14.8%)	157	123 (78.3%)
11	35	12 (34.3%)	54	23 (42.6%)	189	135 (71.4%)
12	48	15 (31.3%)	66	29 (43.9%)	224	154 (68.8%)
13	50	15 (30.0%)	66	33 (50.0%)	238	188 (78.9%)
14	58	18 (31.0%)	91	34 (37.4%)	278	203 (73.0%)
17	104	31 (29.8%)	101	55 (54.5%)	216	181 (83.8%)
18	103	40 (38.8%)	120	62 (51.7%)	186	146 (78.5%)
19	98	38 (38.7%)	135	71 (52.6%)	175	129 (73.7%)
20§	—	—	308	73 (23.7%)	340	129 (37.9%)
21	102	25 (24.5%)	171	60 (35.1%)	195	102 (52.3%)

*Total school population, 122.
†Total school population, 492.
‡Total school population, 577.
§Snowstorm occurred on this day.

The data presented above offer some evidence of the reliability of absenteeism reports as an indication of the prevalence of influenza. Whatever the reason for the observed differences in the percentage of absenteeism due to influenza among the three schools, it appears that total absenteeism is sometimes a poor index of the prevalence of influenza.

Some information concerning the occurrence of subclinical infection with influenza B virus has been acquired from previous studies. Stuart-Harris et al.[13] reported the cases of several patients who developed neutralizing antibodies following exposure to influenza B infection and remained symptom free. In 1944 Francis[14] reported that 11 of 30 uninoculated controls without recognizable illness developed a significant rise in antibody level after a period of 14 days.[14] During the course of an epidemic of influenza B infection in a mental institution, Nigg and her associates[6] found that 14 per cent of blood specimens taken from 77 contacts who had not been ill showed positive complement-fixation reactions for influenza B virus in a dilution greater than 1:5.

In the present study significant rises in antibody titers for the influenza B viruses were demonstrated only in the blood of persons who had characteristic symptoms of infection. Identical results in this respect were shown in most cases both by the complement-fixation reaction and by tests for inhibition of chicken red-cell agglutination.

The apparent disparity between this and the previous studies noted above may have been a matter of strain peculiarity. It must be recalled, however, that the sample studied was small and that virus isolation was not attempted on healthy contacts. At any rate, significant antibody responses were demonstrated only in patients with clinical evidence of infection, and the existence of healthy carriers could not be postulated on the basis of serologic evidence alone.

It is noteworthy that of 19 persons considered to be ill with influenza, laboratory studies confirmed the clinical diagnosis in 16. In only 3 cases, all of which occurred in one family, did serologic tests fail to tally with the clinical impression. Although serologic studies were performed on a relatively small number of patients, it is reassuring that confirmation of the clinical diagnosis was obtained in a high proportion (84 per cent) of the cases studied in the laboratory. The uniform clinical picture manifested by the majority of patients and the sharp epidemic curve observed in the three schools and in the individual grades of the junior high school are further evidence that a single etiologic agent was responsible for this outbreak.

Summary

During the course of an epidemic of influenza B infection reported in 1945 from many areas in and outside the United States, a sharp outbreak occurred in Needham, Massachusetts. An epidemiologic and laboratory investigation was carried out in an elementary school and in the junior and senior high schools.

From December 2 to 21 a total of 484 cases of influenza occurred in the three schools, the attack rate per 100 pupils being 53.7 in the junior high, 44.7 in the elementary school and 24.4 in the senior high school. The distribution of cases by day of onset indicated a sharp epidemic curve in each of the three schools and in the individual grades of the junior high school. The day of highest incidence in the junior high school preceded that in the senior high and Avery schools by a week.

The attack rates in individual classrooms in the junior high school varied from 38.5 to 82.9 per cent. In seventeen classrooms in the junior high school, the attack rate was 50 per cent or higher in nine and less than 40 per cent in only three.

Comparison of total absenteeism with that due to influenza during the course of the outbreak revealed marked differences among the three schools. In the junior high school, where the attack rate was highest, influenza was responsible for the greater part of the total school absenteeism. In the remaining two schools many children absent from school did not have influenza. The reliability of absenteeism as an index of the incidence of influenza is at times open to question.

Two strains of virus were readily isolated from cases in Boston, and a third strain was isolated from one of the Needham cases. These three epidemic strains were identified as influenza B viruses.

Of 19 typical cases of clinical influenza in Needham, serologic evidence of influenza B infection was obtained in 16. All asymptomatic contacts failed to show a rise in titer of antibodies for the influenza A and B viruses.

The confirmatory laboratory evidence, the uniform clinical picture manifested by the majority of patients and the sharp epidemic curves noted in all three schools suggest that a single etiologic agent was responsible for this outbreak.

We are indebted to the following officials of Needham for their assistance and for making this study possible: Berwood A. Newman, Superintendent of Schools; Robert McClellan, Health Officer; Rose M. Mayers, R.N., Board of Health Nurse; and Marion Maxwell, R.N., School Nurse.

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MEDICAL PROGRESS

PEDIATRICS*

MEMBERS OF THE STAFFS OF THE CHILDREN'S AND INFANTS' HOSPITALS†

BOSTON

THE justification for considering pediatrics a specialty does not arise from its concern with a particular type of disease or with the special technics necessary to deal with a particular region of the body, but rather from the nature of its patients, who are distinguished by an outstanding characteristic — *they are constantly growing*. The aim of the pediatrician is to assist, to the limit of his abilities, this process of growth so that his patient may increase "in wisdom and in stature." Thus, the basic goal of pediatrics is preventive, although it is concerned with curative medicine and surgery, and its scope naturally extends from the time of conception until the cessation of physical growth. This broad view has added to the concerns of the pediatrician the antenatal period on the one hand, when he must work with the obstetrician, and the period of adolescence on the other, when his interests begin to merge with those of the internist and gynecologist.

By the application of knowledge in the fields of nutrition and infectious disease, pediatricians and public-health workers have been remarkably successful in assisting the physical growth of children. This success only emphasizes their obvious failures. Accidents, particularly those due to automobiles, are the major cause of death in childhood, and yet physicians and public-health workers have given their prevention little thought. It is in the guidance of mental and emotional development that the shortcomings of present knowledge and practice are most apparent. The ultimate standard by which the success or failure of pediatrics must be judged is the extent to which its charges become well integrated, responsible citizens when they graduate to adult life. The prevalence of psychoneurotic disorders as a cause of rejection in Selective Service examinations and of disability in American troops has clearly indicated deficiencies in the field of mental hygiene.[1] Success in this field will depend, as it does in that of physical hygiene, on a basic understanding of the normal pattern of growth and development.[2, 3]

Although the care of both healthy and sick human beings in the growth period has become the special concern of pediatrics, it is doubtful whether there are sufficient pediatricians to provide for more than a fraction of the child population. The extent to which present facilities for the medical care of children are adequate and to which services to children are provided by pediatricians, by general practitioners or by other types of professional workers will be known when the present study of child health services[4] is completed. This study, organized by the American Academy of Pediatrics, with the co-operation of the Children's Bureau and the United States Public Health Service, represents a laudable attempt by a voluntary medical organization to obtain the necessary information on which to base future plans for the improvement of medical care.

It is debatable whether the attempt should be made to provide pediatricians for all children. In society the unit is not the child but the family, all of whose members are involved whenever illness strikes anyone in the group. It is interesting to compare the emphasis on specialization in this country to the policy in Great Britain, where, traditionally, the pediatricians have been a small group of consultants, routine child care being given on the preventive side by public-health workers and on the curative side by general practitioners. In a recent report, the Pediatric Committee of the Royal College of Physicians of London[5] states:

> The present policy of having two groups of medical personnel, the one engaged in preventive and the other in curative work, is good neither for the child nor the doctor. A long-term policy should aim at making the general practitioner primarily responsible for the medical care of the child, in both the prevention and treatment of disease, since he is the one best fitted to give this service in the home.
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> Ultimately, the normal channel through which the family seeks medical advice in health as well as the sickness should be by consultation with the family general practitioner.

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Consequently, the skill in pediatrics of the general practitioner must be adequate so he can play this essential role in child health particularly in the home.

This review is written primarily for those general practitioners whose all-important work includes the care of infants and children. We have chosen to stress the preventive side of pediatrics because it occupies such a large part of the efforts of physicians engaged in pediatric practice. Certain fields, in which recent advances have been little short of miraculous, such as the surgical correction of congenital anomalies of the gastrointestinal tract or cardiovascular system, should be mentioned, but have merited separate reports.[6–8] The availability of methods for the repair of these congenital defects places an additional burden of responsibility on the general practitioner for their early recognition. Of even greater interest is the accumulation of knowledge concerning the pathogenesis of these defects, since it points the way toward their prevention. This will be apparent in the following sections.

Prenatal Pediatrics

Information related to the nonhereditary processes affecting the child in utero is still largely in the speculative stage. Exact details have not been explored, except in the matter of maternal and fetal blood incompatibilities, which will be the subject of another report.[9] Progress in a few other matters of prenatal influence is briefly discussed below.

It has been clearly shown by Miller et al.[10–12] and by others[13] that the infants of women who are, or who later become, diabetic present a collection of anatomic peculiarities acquired before birth. In association with these abnormalities the fetal and neonatal mortality is about 20 per cent, or six times the expected rate for normal pregnancies. This mortality is no less in pregnancies five years before the onset of the mother's diabetes than it is once diabetes has made its clinical appearance. Even ten to twenty years before this event, the fetal and neonatal loss is about three times that expected in women who do not later become diabetic. The fetuses and infants show one or several of the following characteristics: increased birth weight, cardiac enlargement, extramedullary hematopoiesis, hyperplasia of pancreatic islets and a tendency toward gross, nonspecific congenital anomalies.

A connection between this perversion of prenatal development and actual or potential maternal diabetes is obviously present, but its mechanism is completely unknown. Certainly, it has nothing to do with maternal hyperglycemia. Miller[12] lists certain reasons suggesting that the primary derangement is one of maternal anterior pituitary secretion. Whatever the explanation, it is apparent that normal women giving birth to infants weighing 9 pounds or more, or to those with unexplained cardiac hypertrophy or with unexplained features suggesting erythroblastosis, should be followed for the later development of diabetes mellitus. Finally, of course, the live-born infant with any of these features should be watched with extraordinary care, since only symptomatic means are available for meeting a definite threat to survival.

The relation of maternal nutrition to the proper development and growth of the fetus has been demonstrated by numerous animal and human studies. Warkany's[14] excellent review of these contributions — many of them his own — leaves little doubt that maldevelopment of the animal fetus may be thus brought about. Whether a large number of human congenital abnormalities have this factor as their basis is a problem not yet solved. Warkany's own experimental production of ocular maldevelopment by a maternal diet sharply limited in vitamin A has been confirmed locally in the past year.[15] Food conditions associated with the recent war might be expected to produce deflection of human fetal growth and development. Butler and his associates[16] were unable to demonstrate any harm to infants born to ill nourished women who had been interned by the Japanese in the Philippines, but the number of their cases was relatively small. A larger group was studied in Holland, where marked general undernutrition of the urban populace occurred during the winter of 1944–1945.[17] A significant increase in the frequency of congenital malformations was not discovered, although the deprivation was stringent enough to reduce the birth weights and birth lengths of infants born during the hunger months. A most striking feature of the Dutch situation was the development of amenorrhea in at least 50 per cent of women, so that the birth rate at corresponding later dates fell to below half the normal. The sharp decrease in births interfered with statistical evaluation of the importance of the small increase in malformations discovered. Perhaps, as Warkany[14] has said, "the most serious malformation that can befall an infant may be never to be conceived at all."

Although the prenatal influence of maternal diet on fetal growth is an actuality, rather delicately balanced circumstances may be necessary for the potential deflection of fetal development in human subjects. Maternal diets both sufficient to allow conception and deficient enough to interfere with fetal development must fall in a rather narrow band of the nutritional spectrum. Long-continued depletion of the mother, as by improper nutrition for months or years before pregnancy, is likelier to be required than dietary deficiency merely during the pregnancy.

Interest and data concerning maternal infection during pregnancy as a cause of ocular, cardiac, auditory, cerebral and dental maldevelopments are accumulating.[18–23] Reports continue to appear from Australia concerning the effects of maternal rubella in the early part of pregnancy.[24–26] At a school for the deaf in Brisbane the average admission rate of 7

children a year rose in 1945 to 48. The mothers of 34 of these children gave a history of rubella in pregnancy.[26] Seventeen per cent of the deaf children in this school had murmurs suggesting congenital heart lesions. Swan and Tostevin[25] recently added 40 more cases of rubella during pregnancy to the two earlier series already studied by them. Of these 40 pregnancies, 37 resulted in malformed infants. In the same communication the authors reviewed 16 other pregnancies marked by measles, mumps, varicella, herpes zoster or scarlet fever. In contrast to the overwhelming evidence of a relation between rubella and malformations, pregnancies associated with the other infections resulted somewhat equivocally. The numerical factors are, of course, such as to make the data on so few cases of limited value. Swan and Tostevin have made the reassuring observations that pregnancies beginning as early as two weeks after maternal rubella are apparently without fetal danger, and that those subsequent to the one complicated by rubella will also result in normal infants.

Among several American reports new and useful approaches to the problem have begun to appear. Cordes and Barber[21] describe the retarded lens development and differentiation of the eye of an embryo removed at the seventh or eighth week from a woman who had rubella a week before artificial termination of pregnancy. Fox and Bortin[22] and Aycock and Ingalls[23] have begun the essential task of tracing every infant whose mother is known to have had rubella during pregnancy. Their combined results, summarized in the most helpful review by the latter authors,[23] give a total of 11 women who developed German measles during the critical first trimester of pregnancy. Eight of the resultant infants were normal, whereas the other 3 were malformed, although in no case did the anomaly affect the eyes or the heart. This group, indicating a hazard of about 25 per cent to the fetus, is too small to allow more than the implication that the fetus can escape involvement.

Several agencies, among them the Massachusetts Department of Public Health[27] and a committee representing various national pediatric societies, with Dr. Herbert Miller as chairman, have begun studies by questionnaire to reach a more definite answer to the problem. Co-operation, which of course includes reporting of negative as well as positive results, is strongly urged on all physicians of whom inquiries will be made. Obviously, to know the fetal outcome in a large group of pregnancies associated with definite rubella will be of much greater value than knowledge of how many mothers of malformed infants had rubella during pregnancy. Under present knowledge and until such data are available, a physician whose patient develops definite rubella during the first trimester of pregnancy is forced to consider most seriously the artificial termination of the pregnancy. There are as yet insufficient data to suggest a like procedure when other infectious diseases occur in early pregnancy.

Prevention of Infectious Disease

Desirability of Exposure to Certain Contagious Diseases in Childhood

During the past few years the philosophy toward the common contagious diseases has markedly changed. Formerly, the appearance of cases of any of the communicable diseases in a group of children resulted in the application of strict quarantine measures to all the contacts. In actual practice such rigid quarantine was rarely successful in localizing an outbreak, but there are stronger reasons for a change in the practice. In the first place, the only protection against these illnesses, which practically everyone must have once in his lifetime, is the immunity that develops as a result of an attack. Secondly, these ailments, like most other infectious diseases, are apt to be much milder in childhood and increasingly serious as the age of the victim increases. Thirdly, the time lost from productive occupation is shorter in childhood and can be better spared. Finally, if the diseases are allowed to remain endemic in the community, devastating and widespread epidemics are prevented.

German measles and mumps provide the strongest argument in favor of childhood exposure. The severity of mumps in adult life, with the frequency of involvement of the gonads, pancreas and central nervous system, is much greater than that in childhood. Although sterility results from bilateral involvement of the testes in the male less often than is customarily supposed,[28] it may occur. Both diseases, notably rubella, have been incriminated as a cause of congenital defects in babies born to mothers who escaped the infections in childhood, only to develop them during the first trimester of pregnancy.[18–27]

Thus, rather than attempt to prevent the spread of chicken pox, measles, German measles and mumps, physicians should encourage them to spread among healthy children. On the other hand, the physician must make it his responsibility to protect patients in whom one of these diseases might have serious consequences. This includes sick or debilitated children, pregnant women, susceptible men who for business reasons cannot afford to be ill and children under three years of age, in whom these diseases may be serious. The importance of assuming this responsibility if one adopts a *laissez faire* attitude in dealing with communicable disease in children is illustrated by a recently reported experience.[29] In a private school with an outbreak of mumps it was decided to allow the epidemic to run its course rather than to quarantine all susceptible contacts of the first case. The disease spread as anticipated among the children,

but unfortunately a number of cases of severe mumps, including several of orchitis and meningoencephalitis, resulted when the virus was carried to nonimmune parents by the children. It should also be stressed that, although quarantine of contacts is not recommended in the group of diseases mentioned, such an attitude cannot be adopted with diphtheria because of its serious consequences.

Immunization

The efficacy of active immunization has been conclusively demonstrated in diphtheria, tetanus and smallpox. Vaccination methods have also been developed for a number of other diseases, against which active immunization appears to have a definite but less clear-cut effect. In many cases — for example typhoid fever and typhus — it is difficult to apportion the credit for control of epidemics between immunization and effective sanitation.

Routine immunization is the responsibility of every physician who takes care of children. A recent progress report[30] presented an exhaustive review of the field of active immunization, so that this report is confined to an attempt to answer the following practical questions:

Against what diseases should children in New England be immunized?
When should immunization be carried out?
What types of preparation should be used?
How often should reinoculation be performed?
What dangers are there in immunization?

Our attempt to answer these questions may appear dogmatic. This is not the intention. There are a number of methods for achieving the same objective, and the factors in each case should be weighed. For example, smallpox vaccination should be the initial immunization procedure in any community where the disease has recently been reported, whereas it can ordinarily be deferred until tetanus inoculations have been given. The essence of good medical practice is flexibility based on an understanding of basic principles.

Vaccination against smallpox is absolutely essential. Cases of the disease continue to occur in the United States, and the freedom from epidemics is mainly due to nearly universal vaccination. It should be performed in the first year, since the incidence of its chief complication, postvaccinal encephalitis, is considerably higher in persons whose initial vaccination is performed in childhood or adult life.[31] Since tetanus has followed vaccination, particularly when tight shields were used,[32] vaccination after the completion of tetanus immunization is sometimes preferred. The principal causes of failure to obtain a reaction is a lack of appreciation that the vaccine is a living virus, which may be inactivated by improper or prolonged storage or by the use of alcohol, iodine or mercurial antiseptics to cleanse the skin. Only a volatile substance such as ether or acetone should be used, and this should be allowed to evaporate before the skin is pricked. All the lymph in the tube should be squeezed on the skin, because the lymph may separate from the glycerin. Revaccination should be carried out routinely when the child first goes to school, again at the age of eighteen and when there is an outbreak of the disease or the person is going to a foreign country. In revaccination the physician should not be satisfied with a negative reaction but should *insist* on an immune, modified or typical response.

Diphtheria is one of the most serious preventable health hazards to children in New England, and hence immunization should be given as early as practicable. The original idea that one could not obtain a satisfactory immunity by inoculations given to infants under six months of age is now undergoing close scrutiny, but it is too early to recommend change of the standard procedure of beginning diphtheria immunization at the age of six months. Formerly, most newborn infants were found to be Schick negative as a result of the passive transfer of maternal antitoxin. Now, however, there is a considerable percentage of Schick-positive persons in the adult population, and their infants will be born without such an immunity. This raises the question of early immunization of the infant or of prenatal immunization of the mother.[33] Unfortunately, adults frequently have severe local and constitutional reactions to diphtheria toxoid, so that immunization of the mother should not be considered until the latter half of pregnancy, when damage to the fetus by a reaction is no longer a real possibility. Until a more satisfactory method for immunization of adults against diphtheria is worked out, physicians should probably adopt the attitude of being alert to diagnose diphtheria infection and of beginning immunization promptly at the age of five or six months. If an infant is exposed to diphtheria, antitoxin should not be given unless clinical diphtheria develops. The choice of agents and times for booster doses of diphtheria toxoid is discussed below under tetanus immunization.

Tetanus immunization should be a routine procedure in childhood for the following reasons: it is an infrequent but dangerous disease; although it rarely occurs in adults except after serious injuries, a large proportion of cases in childhood follow injuries and infections so mild that the patients are unlikely to seek medical advice[34]; the use of tetanus antitoxin may sensitize the patient to horse serum, making it difficult to administer diphtheria antitoxin subsequently; and if the patient has been immunized against tetanus, the physician is spared the frequently difficult decision regarding the advisability of administering tetanus antitoxin for many of the minor cuts and injuries in childhood.

Immunization of children against both diphtheria and tetanus can be carried out with combined toxoid with good results and few reactions.[35] Adolescents and adults are much less liable to severe reactions to tetanus than to diphtheria toxoid, which is fortunate since the immunized person should receive a booster dose of 0.5 to 1.0 cc. of tetanus toxoid if he sustains a severe injury that is likely to lead to tetanus. Primary immunization with combined toxoid should be given at the age of six months. Fluid toxoid requires three doses spaced at intervals of two to four weeks, and alum-precipitated toxoid two doses spaced at an interval of two to four months. A disadvantage of the latter is the occasional development of sterile abscesses and the somewhat greater frequency of sensitization to certain components of the toxoid due to the marked adjuvant effect of alum on sensitization. A booster dose of 0.5 cc. of the combined toxoids should certainly be given at the age of five years when school starts and perhaps at two years as well, owing to the increased prevalence of diphtheria.[30, 36]

Vaccination against pertussis is effective in diminishing the incidence and severity of the disease provided an adequate dose of properly prepared Phase I vaccine is used.[37] If reactions to pertussis vaccine were not relatively frequent and occasionally severe, there would be no hesitation in recommending its universal administration in infancy. The hazard of the disease is principally in the first year of life, and if, as Sauer[38] maintains, immunization should not be started before the age of six months, immunity will not be established until the age of nine or ten months. Recent studies, however, suggest that early immunization can establish adequate antibody levels if alum-precipitated vaccine is used.[39, 40] If infants are kept at home during the first year, they will not often be exposed without the knowledge of the parents or physician. The administration of hyperimmune human serum,[41] hyperimmune rabbit serum[42] or concentrated human hyperimmune globulin[43] in adequate doses to exposed infants should give passive protection and will usually ameliorate the disease if it develops.[44] The introduction of streptomycin affords another potential method of treating the disease. In view of all these facts, the use of pertussis vaccine as a routine procedure is somewhat less urgent than formerly but should be encouraged whenever there is a real risk of exposure, particularly in infants in families with a number of older children in school, since pertussis is a serious disease in infancy. In children who have been immunized to pertussis and who are exposed to the disease after six months or more a booster dose of 1.0 cc. subcutaneously is recommended. With the general use of pertussis immunization, school quarantine measures should be eliminated,* since many immunized children escape infection or have unrecognized mild attacks of the disease.

There has been a steady increase in the practice of using combined antigens for routine inoculations.[45] Combined diphtheria and tetanus toxoid has much to recommend it. Combinations of these two toxoids with pertussis vaccine, either in a fluid state or absorbed on aluminum hydroxide, are available. The advantage of these triple combinations lies in the reduction of the number of injections. When alum precipitation was used with pertussis vaccine, the reaction rate appeared to be increased, but there is insufficient published evidence for an evaluation of the newer aluminum hydroxide preparations.[46] One reason to question the general use of these triple combined vaccines is psychologic. Immunization with the two toxoids is essential. Reactions are chiefly due to the pertussis vaccine, and with triple vaccines, the occurrence of severe reactions may discourage completion of the course of immunization and discredit the diphtheria toxoid that every child must have.

There are no other vaccines that should be given serious consideration for routine use in children in New England. Influenza A and B vaccine has been proved to diminish the attack rate of epidemic influenza in outbreaks due to both A and B types of virus.[47, 48] Its use in children, however, seems hardly worth while. Influenza, like other infectious diseases, is milder in childhood than in adult life. Since the duration of immunity from vaccination is probably short, reactions to the various types of vaccines are often considerable and the development of hypersensitivity to egg protein is a possibility, there is something to be said for permitting children to acquire a basic immunity by natural infection with the virus, which may afford some degree of protection to the inevitable exposures in later life.

Scarlet-fever immunization has enjoyed a varying vogue. Since protection is produced only against the toxin and not against infection with the hemolytic streptococcus its value to the child is open to question. Moreover, reactions with the standard plan of toxin injections are often considerable and even dangerous. Since severe, toxic scarlet fever rarely occurs today and penicillin therapy adequately controls the septic aspects of streptococcal infection, there is little justification for immunization at present. The intradermal injection of a tannic acid precipitated toxin may obviate some of the objections to scarlet-fever immunization.[49]

The question of immunization against typhoid fever, typhus, cholera, plague and yellow fever may arise in children going overseas to join their families in Europe and Asia. It should be emphasized that, with these diseases, immunization is only one of the important measures necessary to prevent the infection. Since the food of the infant can be sterilized by an intelligent mother, there appears to be little need for cholera or typhoid injections before six

*Families, however, should be notified of the presence of pertussis or other contagious diseases in the school so as to permit the protection of vulnerable persons, such as newborn babies, by isolation or passive immunization.

months of age. So far as plague and typhus are concerned, however, it is equally essental for the mother to know the endemic status of the disease in her area and to make sure that nursemaids, cooks and so forth are not carriers of the insect vectors involved. In general, the vaccines against typhoid fever, plague, cholera and typhus may be given to children by the same schedule as that for adults, half the adult dosage being used for children under five years of age. It should be remembered that stimulating doses must be given every six months for typhus and every four months for cholera and plague, and that immunization should be completed two weeks before the subject enters an endemic area.[50] The chance of exposure of infants to yellow fever is slight in urban areas, but immunization should probably be given when it is recommended by local health authorities, since lasting protection is thereby afforded.

TABLE 1. *Mortality among Patients Contracting Tuberculosis in Childhood.*

AUTHOR	TYPE OF INSTITUTION	AGE AT DISCOVERY OF TUBERCULOSIS	SUBSEQUENT MORTALITY FROM TUBERCULOSIS
		yr.	%
Tortone[47]	Preventorium and case finding	1	10
		1-2	4
		3	3
Brailey[48]	Hospital and out-patient department	3	14
Smith[49]	Infants' hospital	2	34

The use of immune serum globulin in the prophylaxis of measles in exposed persons has become an established pediatric procedure. A dose of 0.1 cc. per pound of body weight will prevent the disease in the great majority of cases, whereas 0.02 cc. per pound of body weight will usually allow the patient to experience a modified attack. The globulin is given intramuscularly and should be administered in the first six days after exposure. The larger preventive dose should be used for children under three years of age or for sick, debilitated and tuberculous children, and modification should be attempted in all other healthy children who have been exposed to the disease. Modified measles, which is less severe and less apt to be followed by complications, probably gives relatively permanent immunity to most children.[51]

The prophylactic administration of chemotherapeutic drugs has a limited but definite place in preventive medicine. Certain groups of children — notably those who have had one or more attacks of rheumatic fever — run a serious risk of recurrence with an increase in cardiac damage if they contract an infection with Group A beta-hemolytic streptococci.[52] Once they have recovered from their original attack of rheumatic fever, there are psychologic objections to removing these children from their normal environment. Since their homes or schools seldom experience a winter without the occurrence of hemolytic streptococcus infection in some member of the group, there is a special risk for these children at home and at school. The use of prophylactic sulfadiazine — in doses of 0.25 gm. twice a day to young children and of 0.5 gm. twice a day to older children and adolescents — throughout the danger season (from October to June) has seemed to be helpful in diminishing the incidence of rheumatic recurrence.[53] The children should be carefully observed for rash or granulocytopenia particularly during the first six to eight weeks, when most of these reactions occur. If sulfadiazine-resistant organisms become more prevalent, this chemoprophylaxis will obviously be less effective, and studies with the use of oral penicillin will be necessary. At the moment its routine use for this purpose cannot be recommended and would be financially burdensome. Unfortunately, the penicillin treatment of established streptococcal infections has not seemed to prevent rheumatic fever or its recurrences or to affect the course of the disease once it has developed.[54, 55]

Children with rheumatic heart disease or with congenital heart lesions, particularly patent ductus arteriosus or patent interventricular septum, should be given penicillin treatment whenever dental extractions or tonsillectomies are performed, in the hope that the development of subacute bacterial endocarditis will be prevented.[56] Ideally, treatment with full doses should be begun forty-eight hours before operation and continued for five days afterward. The responsibility of keeping the teeth of these patients in good condition is particularly great for the same reason.

The family physician is the person who can do most to control tuberculosis in childhood. The serious prognosis of primary tuberculosis in infancy is indicated in Table 1. The suspicion of tuberculosis in any adult in a home with children should immediately be followed up with x-ray examination. Now that milk is no longer a serious source of infection, tuberculosis in infants and children is almost invariably the result of household contact with an adult who is spreading tubercle bacilli.[60] The only way to prevent tuberculosis is to find all persons with positive sputums and remove them from contact with children. With the Vollmer patch test,[61] tuberculin testing can be carried out routinely in children at intervals of a year, starting at six months of age. The emphasis, however, should be on the discovery of the adult who is the source of the infection, *before* the children become infected rather than afterward.

No discussion of the prevention of infectious disease in children would be complete without mention of the fact that hospitals remain discouragingly dangerous places for infants and children. Transmission of virulent bacteria from one child to another and from attendants takes place all too frequently. Epidemic diarrhea has proved to be even more readily communicable than the ordinary

bacterial respiratory infections. It is possible to diminish the bacterial content of air by the use of ultraviolet irradiation,[62] by the vaporization of glycols[63] and by treating floors and bedding with oil to make bacteria and dust adhere.[64] Nevertheless, the rigid observance of strict isolation technic is an absolute necessity in the care of sick infants in a hospital, if the number of cross infections is to be reduced. Children with diarrhea, draining ears, acute respiratory infections and skin infections (impetigo or eczema) should be rigidly isolated in single rooms whenever possible.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33231

PRESENTATION OF CASE

First admission. A twenty-three-year-old machinist entered the hospital two months after he had been rejected by his Selective Service board because of hypertension.

The patient had been in perfect health until a year before entry, when he began to have a "tired feeling" and discomfort in the low back, which he attributed to overwork and long hours of standing; it occurred about once in three or four weeks and was relieved by rest. At the same time frontal headaches also developed, occurring about once a week and lasting four or five hours. Six months before entry he first noticed easy fatigability.

The patient was in good physical condition but appeared apprehensive. The fundi showed borderline blurring of the disks and diffuse narrowing of all the retinal arteries; there was little arteriovenous nicking. The diastolic blood pressure in the retinal arteries was 65. There was a loud, snapping aortic second sound, and a blowing apical systolic murmur, which was not transmitted. The pulse was bounding. Examination of the lungs and abdomen was negative.

The temperature, pulse and respirations were normal. The blood pressure was 245 systolic, 160 diastolic.

Examination of the blood showed a hemoglobin of 87 per cent and a white-cell count of 11,250. The nonprotein nitrogen was 38 mg., and the cholesterol 170 mg. per 100 cc. A blood Hinton test was negative. The urine gave a ++ test for albumin, but the sediment did not contain cells or casts. A phenolsulfonephthalein test showed 51 per cent excretion of the dye in 2 hours. The maximum specific gravity in the urinary concentration test was 1.018.

X-ray films of the chest showed a cardiothoracic ratio of 12.5:28.5. The left ventricular area was somewhat blunted, and the aortic knob slightly more prominent than normal. An intravenous pyelogram showed little dye excretion on the right; this was repeated and confirmed. The left kidney appeared normal. There were some calcified pelvic arteries. A retrograde pyelogram was normal.

An electrocardiogram showed a normal rhythm, a rate of 85 per minute and a PR interval of 0.16 second. The T waves were inverted in Lead 3, low and notched in Lead 4 and low in Lead 1. A sedation test reduced the blood pressure to 150 systolic, 110 diastolic.

A left lumbodorsal sympathectomy was performed with removal of the sympathetic trunks from the fifth dorsal to the second lumbar segment inclusive. Following the operation the patient developed a serosanguineous effusion in the left side of the chest but recovered satisfactorily and was discharged on the forty-first hospital day.

Second admission (three weeks later). The patient was readmitted for a right lumbodorsal sympathectomy.

At operation the right kidney was found to be grossly normal, but a biopsy was reported as showing nephrosclerosis, Grade III. At discharge the blood pressure while the patient was standing was 165 systolic, 110 diastolic.

Final admission (four years later). The patient was followed in the Out Patient Department. Six months after discharge the blood pressure had returned to 230 systolic, 140 diastolic. He felt well, however, and the headaches had almost disappeared. Eight months after discharge he returned to work. Two years before entry the main complaints were lack of libido and insomnia. He worked eight hours a day and experienced fatigue only after particularly great effort. The blood pressure when the patient was lying down was 240 systolic, 135 diastolic. The insomnia was finally controlled with phenobarbital. Potassium thiocyanate was used to treat the hypertension but was discontinued by the patient because of postprandial pains across the chest and down the left arm to the elbow. A year and a half before entry he began to have episodes of precordial "squeezing" sensations, occasionally radiating down both arms and occurring several times a month when he was walking or climbing stairs or after eating. After a few minutes of rest the feeling disappeared. The blood pressure at that time was 270 systolic, 170 diastolic, and he was occasionally found to have a gallop rhythm. His working time had been reduced to six hours. Five months before entry a chest film showed a cardiothoracic ratio of 14:29, as well as some prominence in the region of the left ventricle.

The lung fields were clear except for some blunting of the right costophrenic angle. An intravenous pyelogram showed prompt excretion of dye on both sides. A phenolsulfonephthalein test showed 63 per cent excretion of the dye in 2 hours. The urine had a specific gravity of 1.020 and was free of albumin. The nonprotein nitrogen was normal. An electrocardiogram showed a sinus rhythm and a rate of 90. The PR interval was 0.17 second, and the QRS complex 0.08. The axis and voltage were normal. There was prominence of the ST segment in Lead 2,

and the QRS complex in Lead 3 was W-shaped. The T waves were upright in Leads 1 and 3 and slightly low in Lead 2; the ST segment in Lead CF_4 was slightly sagging, and the T wave was diphasic.

Three months before entry there was a marked increase in the substernal discomfort. Attacks of steady, crushing substernal pain radiating down both arms, into the back and up the neck to the jaw were brought on by slight exertion, occurring about once a day and lasting about fifteen minutes at a time. A month later the patient developed a cough that was productive of white mucoid sputum and was particularly severe at night. A month before entry he was forced to stop working. The attacks had begun to occur even while he was resting, and he sometimes awoke with the sensation in the morning. The pain was so severe that he always had to stop whatever he was doing until it had subsided. At the time of entry he was having as many as four attacks a day and was practically bedridden. Mannitol hexanitrate was of no avail. Nitroglycerin gave some relief but was followed in several hours by nausea and vomiting.

Physical examination disclosed an anxious patient who was repeatedly belching small quantities of air. The left fundus showed an occlusion of the superior temporal artery just off the disk, as evidenced by parallel ensheathing of the arterial walls for a distance of 1 or 2 disk diameters. Otherwise the vascular changes appeared if anything less severe than those on the first examination. The left border of the heart was in the anterior axillary line in the fifth and sixth interspaces. The aortic second sound was much louder than the pulmonic second. There was a questionable apical gallop. The lungs and abdomen were clear.

Examination of the blood showed a red-cell count of 5,310,000, with 15.0 gm. of hemoglobin, and a white-cell count of 9200, with 80 per cent neutrophils. The urine had a specific gravity of 1.020 and gave a ++ test for albumin.

An electrocardiogram showed a sinus rhythm at a rate of 90 per minute. The S waves were sagging in Leads 1 and 2, and the T waves were sagging, low and diphasic in Leads 1 and 2, upright in Lead 3 and inverted in Lead CF_4; the ST segment was sagging in Lead CF_4.

On the second hospital day, during a bed bath, the patient suddenly complained of dizziness and lapsed into unconsciousness. When a physician arrived two minutes later the heart had ceased beating, and the patient was somewhat cyanotic. He emitted several gasps during the following three minutes. Despite the intracardiac administration of coramine the heart action could not be re-established.

Differential Diagnosis

Dr. Edward F. Bland: This is in some respects a discouraging case but an important one. The patient died at twenty-seven years of age. At the age of twenty-three he had, by most criteria, malignant hypertension — at least, it was acute and severe, and there was beginning retinitis and choking of the optic disks. Renal function was somewhat impaired, although the concentrating power of the kidneys was good. If a patient with this situation appeared again tomorrow, we should consider him a candidate for an almost emergency sympathectomy. There may be some dissenting voices, however, on that score.

In looking back over the record, we are most interested in the evidence whether or not sympathectomy had any effect on this patient's subsequent course. The chief complaint on the first admission was headache; he was largely relieved of this symptom. It has been noted in many cases after sympathectomy, even though the high blood pressure in some cases has been only slightly or moderately ameliorated, that the relief of troublesome headaches has been striking. Furthermore, it is of special interest that four years later the renal function actually seemed a trifle better and the eye grounds were no worse; some observers even thought that they were better. In other words, it seems as though the sympathectomy, without influencing significantly the level of the blood pressure, had in some fashion protected both the eyes and the kidneys. A final point — if we can consider this clinically malignant hypertension, without necrotizing renal arteriolitis by biopsy — is that a twenty-three-year-old patient would have been expected to succumb in a few years in uremia. He died four years later, but not in uremia.

Is there anything that we need say about the differential diagnosis? In any person of this age with hypertension one should consider coarctation of the aorta, but presumably he did not have that. Nothing is said about the arterial pulsations in the legs or notching of the ribs on x-ray study, but almost certainly if abnormal these would have been mentioned. A condition that might be considered in passing is a paraganglioma. The hypertension was not paroxysmal, but we know that perhaps 10 per cent of patients who have hypertension secondary to paraganglioma have sustained hypertension. If such a lesion had been present it would probably have been discovered at operation, since it is routine to search carefully for these tumors; they are not always found in the immediate vicinity of the kidney, however. We are not told the reaction of his blood pressure to change in posture. Dr. Smithwick* has recently pointed out that if the hypertension is due to a tumor of this type the blood pressure falls in a striking fashion when the patient shifts from a recumbent to a standing position. He has studied only a few cases, but that seems to be the pattern. In the case under discussion we have no reason to think that the hypertension was secondary to tumor.

*Smithwick, R. H. Unpublished data.

The final condition that we might consider is primary renal disease on the basis of pyelonephritis in the past, with renal injury. We have no real evidence to suggest this. The retrograde pyelograms showed no irregularity in contour of the ureters, pelves and calyxes, and there was no indication of chronic renal infection. Therefore, we must dismiss these other possibilities and say that this was a case of essential hypertension occurring acutely and severely in a relatively young person. He ultimately died of severe angina pectoris on the basis of coronary disease. At the final admission he did not live long enough to have special studies or therapy instituted. I suspect that those in charge were at somewhat of a loss regarding just what therapy to institute. In addition to nitrites and oxygen, he was probably given digitalis, because of the cardiac enlargement and weakness (gallop rhythm). If he had survived long enough it might have been helpful to have him on a rice diet or at least on a low-sodium regime. If he had improved a little on that and yet continued to have intractable angina pectoris, one might have seriously considered a thoracic sympathectomy for relief of pain.

The cause of this patient's sudden exitus was almost certainly cardiac and not cerebral. It was too abrupt for a cerebral accident. The heart was not beating when the physician, who presumably was nearby at the time, arrived a moment later. Perhaps acute coronary insufficiency is as good an explanation clinically as anything else. For a final diagnosis I believe that he had severe essential hypertension, hypertensive and coronary heart disease and angina pectoris decubitus. He ran a progressively downhill course, so far as the hypertension and coronary disease are concerned, and yet I am forced to think that he received some benefit from the sympathectomy regarding protection of the kidneys and eyes and certainly relief from headaches. Whether or not it was worth while in this case is debatable, but I should strongly recommend the same procedure if faced with a similar situation.

Dr. Robert S. Palmer: Dr. Bland has summarized this case extremely well. In young patients like this, with a high diastolic pressure and early papilledema, we have seen the best results from sympathectomy, provided that cardiac and renal functions are seriously impaired. There have been 3 such patients, three to five years after operation, with normal or nearly normal blood pressures. Two other similar patients, who were considered to have malignant hypertension when operated on three and five years ago, are alive and working, although again hypertensive. One is working in a grocery handling heavy goods. Unfortunately, persistent high diastolic pressures are often associated with diffuse arteriolar disease. There was some evidence of this in the case under discussion. I think that this patient was probably relieved, that his life was prolonged and that the renal function may have been spared. Dr. Bland mentioned emergency sympathectomy. Delay may be costly, since renal damage may advance rapidly, seemingly in a matter of days. I think that I have seen the entire course of malignant hypertension from symptomatic onset to death in five or six weeks. Rarely, there may be such a thing as emergency sympathectomy to spare kidney damage.

Dr. Benjamin Castleman: How often have you seen the onset of angina following sympathectomy in patients who have never had it before?

Dr. Palmer: I do not know. This is certainly an outstanding example. I have had the impression that some people with dorsolumbar sympathectomy and resulting postural hypotension have been relieved of angina even when high dorsal sympathectomy was not done, but I cannot speak definitely on this point.

Dr. Walter Bauer: What right have you to say that sympathectomy will prevent irreversible uremia? There are many other reasons to prevent irreversible kidney lesions.

Dr. Palmer: If I said what Dr. Bauer says I did, it was a brash statement, and I am glad to be corrected. If the patient is operated on, the operation should be done before serious impairment of renal function sets in. It seems that some of our patients, closely similar to this, have continued a long time without progressive kidney change, whereas patients with malignant hypertension who have not had sympathectomy, as Dr. Bland has pointed out, often have progressive changes in the kidneys and die in uremia. I should point out that it is remarkable for a person with this type of hypertension to have gone so long without more kidney damage. I am not sure, from the qualitative tests of renal function, that positive improvement in renal function was demonstrated.

Dr. Tracy B. Mallory: Dr. Evelyn, will you express your views on the subject?

Dr. Kenneth A. Evelyn: In this case, as in many similar cases that have been reported in the literature, I find it difficult to accept the evidence brought forward in support of the claim that sympathectomy has a specific ability to relieve headache even in patients in whom the operation fails to produce a significant lowering of the blood pressure. It is well known that relief of symptoms in hypertensive patients may occur after a variety of nonspecific therapeutic measures, including venesection and psychotherapy, but when there has been no reduction of blood pressure it does not seem justifiable to ascribe any specific virtue to sympathectomy in this regard. In any event, in this particular patient, headache was a relatively minor complaint even before the operation.

My second comment concerns the diagnosis of malignant hypertension in this patient and the validity of Dr. Bland's suggestion that the sympa-

thectomy might be given credit for having exerted a protective action on the kidneys, because the patient did not develop progressive renal failure. It is true that death in uremia with the post-mortem finding of necrotizing renal arteriolitis is the expected end-result in patients who conform to Fahr's original criteria for the diagnosis of malignant hypertension, but this unfortunate term has been redefined in so many different ways during the past twenty years that there are now no generally accepted minimum criteria for a clinical diagnosis of malignant hypertension. In this case, the diagnosis seems to have been based mainly on the patient's age and the finding of "questionable blurring of the optic disks." Even if the diagnosis of malignant hypertension is accepted, however, it does not seem justifiable to assume that the untreated course would inevitably have led to progressive renal failure, and therefore to suggest that sympathectomy exerted a protective action on the kidneys because renal failure did not occur. On the contrary, it seems to me that there is nothing in the history of this case that is incompatible with the assumption that the operation had no significant beneficial effect on the progress of the disease, which ran a fairly rapid course from accidental discovery to death in a period of four years.

In conclusion, I should like to make it clear that my remarks are not intended to convey the impression that sympathectomy should not have been performed on this patient, or that it should not be given a trial in other cases of a similar nature. On the contrary, the shortcomings of other methods of treatment are so obvious that it seems perfectly reasonable to proceed with the operation, merely because one can offer little else that may be expected to exert a beneficial effect on the course of the disease. I believe, however, that we can hope to arrive at an accurate evaluation of the real therapeutic effectiveness of sympathectomy in the treatment of hypertension only if we analyze the results in each case with the maximum degree of objectivity.

Clinical Diagnoses

Malignant essential hypertension.
Hypertensive heart disease.
Cardiac arrest.

Dr. Bland's Diagnoses

Essential hypertension, severe.
Hypertensive and coronary heart disease.
Angina pectoris decubitus.
Lumbodorsal sympathectomy.

Anatomical Diagnoses

Arteriosclerosis, coronary, severe, with extreme narrowing.
Cardiac hypertrophy and dilatation, slight.
Myocardial infarcts, focal, old and recent.
Arteriolar nephrosclerosis, severe right, minimal left.
Arterial and arteriolar sclerosis, generalized, moderate.
Operations: bilateral lumbodorsal sympathectomy, old.

Pathological Discussion

Dr. Mallory: Interest naturally centers on the histologic findings in the kidneys. At the time of the sympathectomy, biopsies were done on both kidneys. It will be recalled that the right kidney had shown possible evidence of impaired function, if the intravenous pyelogram is to be credited. Later, however, the dye excretion improved on that side. The biopsy of the right kidney showed quite marked arteriolar changes, which we classified as Grade III, whereas the biopsy from the left kidney showed only Grade I changes. At autopsy the same degree of difference was apparent on the two sides, although there was progression of both. Even the more severely involved kidney showed no necrotizing arteriolitis.

The other findings were approximately as expected. The heart showed moderate hypertrophy, weighing 430 gm. The major coronary arteries were severely sclerotic, and the lumens reduced to pin points — in some places there was no lumen. There was no major infarction of the heart, but the myocardium presented evidence of some focal old scarring and also evidence of numerous small spots of fresh necrosis of cardiac muscle that had the appearance of being two to four days old. This fresh necrosis coincided with the period of terminal entry to the hospital. The lungs showed chronic passive congestion.

CASE 33232

Presentation of Case

A forty-nine-year-old man entered the hospital because of retrosternal and epigastric pain.

Three and a half hours before admission, during a heated argument, the patient was suddenly seized by a pain in the neck, at about the level of the thyroid cartilage. He was forced to sit down and was unable to talk or breathe properly for about fifteen minutes. During that time the pain gradually traveled downward anteriorly in the midline to the upper abdomen and finally settled in the left upper quadrant, radiating through the body to the angle of the left scapula. It remained constant in the retrosternal and abdominal location, until the time of admission. No nausea, vomiting, hemoptysis or other symptoms accompanied this attack. Three days prior to admission the patient had slipped and fallen on a curbstone, with considerable resulting pain and ecchymoses and swelling of the left leg. In addition, for ten days he had had a slight cough productive of whitish sputum in which there were occasional small amounts of blood.

At the age of nine years there had been an attack of rheumatic fever, allegedly with cardiac involvement, which had lasted three months. There were no recurrences. Before his illness, the patient's weight had been normal; afterward, he began to gain and at fourteen years of age weighed 216 pounds.

At the time of admission, the patient was sweating and rolling from side to side with pain. Extreme obesity — the patient weighed 270 pounds — made physical examination difficult. There were bilateral cataracts. The heart and lungs were normal. There was slight tenderness in the left upper quadrant near the costal margin. The abdomen was soft; no organs or masses were palpable. A large contusion covered the anterior surface of the left leg from above the knee to the mid-tibia. There were many superficial varicose veins over both legs.

The temperature was 100°F., the pulse 82, and the respirations 16. The blood pressure was 190 systolic, 120 diastolic.

Examination of the blood revealed a hemoglobin of 16.5 gm. per 100 cc. and a white-cell count of 10,400, with 83 per cent neutrophils. The urine contained no albumin. In the sediment there were 1 to 3 red cells and an occasional white cell per high-power field. In the x-ray film of the chest, the lungs appeared clear. The heart was enlarged and the aorta tortuous (Fig. 1). An electrocardiogram on

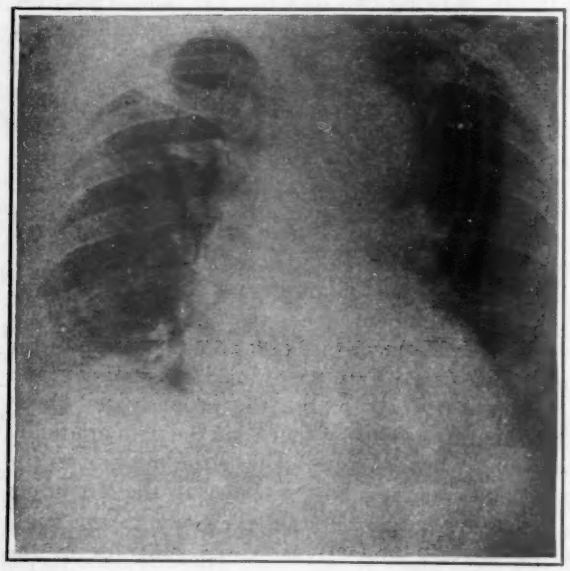

FIGURE 1.

admission and another five days later showed changes consistent with left-axis deviation; no indication of infarction was observed in either film. Shortly after admission the serum amylase level was 20 units, and the nonprotein nitrogen 23 mg. per 100 cc.

On the morning of the second hospital day the general condition appeared improved. Gas and feces were passed freely. Despite morphine and Demerol, the abdominal pain persisted steadily. By evening the temperature had risen to 101°F., remaining between 99.5 and 101° therafter. By evening the pain had progressed down the abdomen below the umbilicus, while persisting in the former locations. The white-cell count rose to 14,800. Rare white cells, red cells and epithelial cells were present in the urine. A repeat chest film compared to that of the first day showed a generalized increase in the pulmonary vascular markings (Fig. 2). A

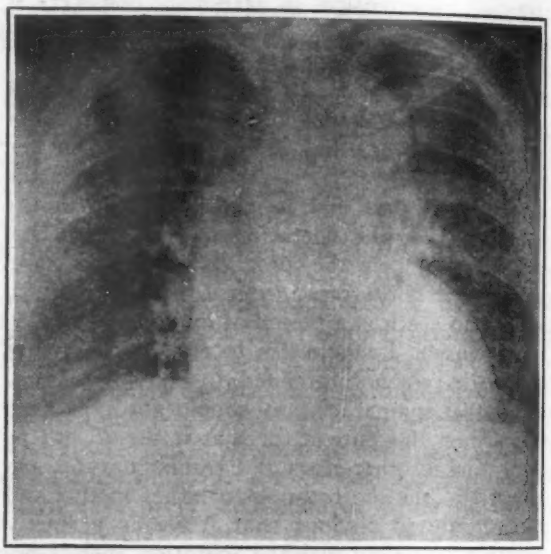

FIGURE 2.

plain film of the abdomen was normal. On the third day no essential change was noted, but occasional extrasystoles with long compensatory pauses were detected. The mitral first sound had a peculiar quality, thought to represent a presystolic murmur, and after some of the extrasystoles there was a mid-diastolic rumble. The pulsations in the dorsalis pedis artery were strong.

No new events occurred until the evening of the fifth day, when the pain became extremely sharp and extended into the epigastrium, up into the neck and back to the epigastrium over a fifteen-minute period. Ten minutes later it again shifted, this time to the sixth intercostal space in the anterior axillary line. The patient was sweating and rolling about in pain. He became cyanotic, pale and cool. The blood pressure fell from 190 systolic, 110 diastolic, at the onset of the episode to 80 systolic, 60 diastolic, at its end, later rising to 120 systolic, 100 diastolic. A chest film showed homogeneous density over nearly the entire left lung field (Fig. 3).

Six hours after the acute attack, the patient complained of throbbing chest pain, became cyanotic and died.

Differential Diagnosis

Dr. Oglesby Paul: In brief, this is the case of a forty-nine-year-old hypertensive man with a background of rheumatic heart disease who, after ten days of cough and hemoptysis and with a three-day-old abrasion of the left leg, entered the hospital with severe pain in the neck, chest, back and upper abdomen. Examination was essentially negative, except for the hypertension and slight left-upper-quadrant tenderness, and after a five-day course he succumbed with an exacerbation of symptoms. On reading the history, one is more impressed by the negative findings than by the positive ones. The lungs were never mentioned as having been abnormal on physical examination; the heart, except for enlargement in keeping with the hypertension and rather questionable evidence of mitral stenosis was not remarkable, and the abdomen was notable for its normal character. The laboratory data revealed only a moderate leukocytosis and a terminal clouding of the left lung field on x-ray study, the latter being the only definitely helpful findings. A low-grade fever was present throughout.

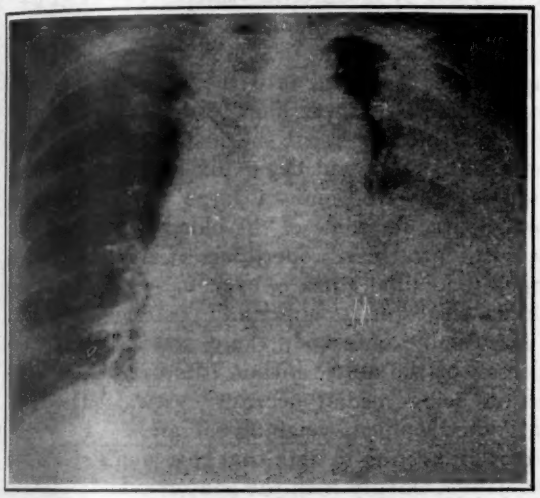

Figure 3.

Several diagnoses that come to mind should be mentioned for the sake of completeness but appear unlikely. The sudden onset of severe chest pain suggests a spontaneous pneumothorax, but the physical and x-ray findings allow us to rule out such a possibility. Mediastinal emphysema may also be eliminated on the same grounds. Pulmonary embolism is suggested by the history of trauma to one leg, by the sudden onset and by the evidence of some disease of the leg veins. Prolonged, severe and widespread pain of this type, however, is not characteristic of that condition, and the absence of tachycardia and dyspnea essentially excludes such a diagnosis. In this patient pain was the cardinal symptom; with embolism to the lung, on the other hand, shortness of breath is usually predominant, and there may be no pain at all. Furthermore, definite evidences of a peripheral phlebitis are lacking, and there were no x-ray signs of pulmonary infarction.

Might not this man have had a myocardial infarct? There are several points in the case history that would seem to make such a condition not the diagnosis of choice. In the first place, as has been often pointed out, the pain associated with myocardial infarction does not typically occur abruptly as in this case but may build up with increasing intensity over a matter of minutes or even hours. Next, one notes the absence of arm discomfort and the presence of back and abdominal pain. Coronary occlusion with myocardial infarction certainly may be accompanied by pain in these last two areas, but perhaps such a complaint is more characteristic of a dissecting aneurysm. During the period of hospitalization no helpful findings, such as pericardial friction rub and electrocardiographic evidence of infarction, appeared. Finally, the past history as given contains no mention of angina pectoris or of previous episodes of pain that might have been interpreted as being of coronary origin.

Could the pathologist have given the medical man a surgical abdomen to discuss? If this man had a ruptured viscus, acute pancreatitis or mesenteric thrombosis, he showed an extraordinarily normal abdomen throughout, in addition to a well behaved intestinal tract, which did not even cause nausea or constipation. I cannot make a purely intra-abdominal diagnosis.

It seems that the one condition that fits this man's illness best is a dissecting aneurysm. He belongs to the right age group for such a diagnosis, and at this hospital, we have encountered more men than women with that diagnosis. The presence of significant hypertension is almost an invariable finding, and as with this man, the blood pressure is often sustained at a high level until the last moments of life. The first dissection in the media of the aorta may result in sudden excruciating and prolonged pain, which may be referred to both the thorax (anteriorly and posteriorly) and the abdomen. It is usual for these patients to survive for a matter of hours or days, rarely even for years, and sudden death at the onset is not found in most cases. The essentially negative physical examination is also consistent with such a diagnosis, and the lack of change in the electrocardiogram is an expected finding. Indeed, a changing electrocardiographic pattern would make one think of something other than a dissecting aneurysm.

I should interpret the terminal episode as one of rupture of the column of blood through the adventitia of the aorta into the left pleural cavity, producing a slow steady leak. The chest x-ray findings might best be explained on that basis. Whether or not the aorta also ruptured into the pericardium I do not know. There is actually no necessity for assuming that it did. The presence of good pulsations in the dorsalis pedis artery bilaterally indicates that the dissection probably did not extend down to the common iliac arteries. I am unable to correlate such a diagnosis with the possibility of rheumatic heart disease and with the history of hemoptysis. The patient could have had mitral stenosis; if so, it must have been incidental and not a factor in the final illness.

I shall, therefore, make a diagnosis of a dissecting aneurysm secondary to a cystic necrosis of the media of the aorta.

Dr. Milford D. Schulz: The films of the chest made on entry show a tortuous and somewhat widened aorta, which can still be traced fairly well to the diaphragm. Twenty-four hours later the mid-portion of the descending aorta has become irregular in outline and is lost in an ill defined shadow that extends to each side of the mediastinum. A film made four days later shows fluid in the left pleural sinus, the mediastinum seems to be slightly wide and irregular, and the descending aorta is completely lost. The widening of the mediastinum, the irregularity of the aortic shadow and the loss of its contour can certainly be explained by hemorrhage into the mediastinum or into the wall of the aorta, which subsequently escaped into the left chest.

Clinical Diagnosis

Dissecting aneurysm of aorta.

Dr. Paul's Diagnosis

Dissecting aneurysm of aorta, with rupture into left pleural cavity.

Anatomical Diagnoses

Dissecting aneurysm of aorta, with rupture into left pleural cavity.

Cardiac hypertrophy, hypertensive type.

Pathological Discussion

Dr. Benjamin Castleman: This man had an aortic dissection. The intimal tear occurred in the arch close to the origin of the left subclavian artery, and the dissection had progressed from this point distally down to but not involving the iliac arteries. There was some dissection up the left common carotid and subclavian arteries but no involvement of the renal or mesenteric vessels. The exact point of external rupture could not be determined, but it was obvious as soon as the chest was opened that the rupture had occurred into the left pleural cavity, because the latter was filled with both clotted and unclotted blood. From the history we know that the external tear had begun six hours before death and was therefore not a large one. There was enough time for some of the blood to extend extrapleurally into the retroperitoneal tissues around the upper abdominal aorta — even to surround the left adrenal cortex on its upper and posterior surfaces.

As usually observed, there was slight arteriosclerosis of the aortic intima, the cause of the dissection being medial necrosis cystica. The heart was hypertrophied, weighing 630 gm.

It is interesting to note that this man's symptoms correlate strikingly with the anatomic findings. The initial tear was in the left arch, with dissection up the left great vessels, and the initial symptom was pain in the neck. The dissection went down the descending aorta, thus accounting for the abdominal symptoms. There was practically no chest pain, which corresponds with the absence of dissection in the ascending aorta, unlike the great majority of cases of aortic dissection, in which the ascending portion is involved.

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The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

ONE HUNDRED AND SIXTY-SIXTH ANNIVERSARY

The one hundred and sixty-sixth anniversary of the Massachusetts Medical Society, held at the Hotel Statler, Boston, on May 20, 21 and 22 was a highly successful affair. The total registration — 1521 — although not so large as that of last year, was impressive, and all who were present, including fellows, speakers, and exhibitors, seemed to be more than satisfied.

The annual meeting of the Council was held on the evening of May 19. Practically all committee reports, together with their recommendations, were routinely accepted on the basis of approval by the Executive Committee. Two matters are of general interest. Dr. Humphrey L. McCarthy, chairman of the Committee to Meet with General Hawley, reported that the scheme whereby medical care to veterans was to have been covered by a contract between the Blue Shield and the Veterans Administration had been blocked. He suggested that the Society deal directly with the Veterans Administration under a gentleman's agreement, similar to the so-called "Kansas Plan," and the motions necessary to reopen the matter were passed by the Council. Under "new business," Dr. Merrill C. Sosman presented resolutions adopted jointly by several groups of radiologists, anesthesiologists and pathologists relative to the all-inclusive coverage of hospital services by the new contracts of the Blue Cross, which became effective on June 1. These organizations oppose any arrangement by a hospital with Massachusetts Hospital Service that permits the latter to guide or determine professional services, oppose the principle of comprehensive coverage on a per-diem basis of compensation because it fails to distinguish between hospital and professional services and recommend that charges for all professional services should be specifically excluded from all hospital-service plans. After the Council had voted to suspend its rules for procedure, approval of these resolutions was voted. The officers elected for the current year are as follows: president, Edward P. Bagg; president-elect, Daniel B. Reardon; vice-president, Charles J. Kickham; secretary, Joseph Garland; treasurer, Eliot Hubbard, Jr.; assistant treasurer, Norman A. Welch; orator, Allen S. Johnson.

At the annual meeting, the retiring president, Dr. Dwight O'Hara, after giving an interesting and inspiring talk covering "The State of the Society," read the names of eleven physicians who had joined the Society in 1897 and who were still active fellows — a delightful courtesy that deserves adoption as an annual custom. After presentation of Dr. Harrison H. Shoulders, president of the American Medical Association, and of the incoming officers, Dr. Leland S. McKittrick gave the annual oration, his topic being "Medical Care in Our Free Society." This address will appear in the June 19 issue of the *Journal*.

The Shattuck Lecture was presented by Dr. William Dock, professor of medicine, Long Island

College of Medicine, and director of the Medical Service, College Division, King's County Hospital, Brooklyn, New York. This paper, entitled "Clinical Significance of Circulatory Peculiarities of Some of the Vital Organs," was published in the May 22 issue of the *Journal*.

The annual dinner was attended by 418 fellows and guests. The principal speaker was Dr. Shoulders, who spoke on the topic, "The Responsibilities of the Medical Profession."

The scientific sessions were well attended, as were the section meetings and the exhibits. The paucity of scientific exhibits was unfortunate but necessitated by a cutting down of the space permitted. It is to be hoped that in the future some arrangement can be made whereby a larger number of such exhibits can be accommodated.

Dr. Sidney C. Wiggin, the other members of the Committee on Arrangements and Mr. Robert St. B. Boyd, executive secretary of the Society, deserve great praise for making possible a meeting that was so successful.

ANTHRAX

Although relatively few physicians have ever seen a case of anthrax in their practices, the disease does occur with enough frequency to constitute a true occupational hazard, particularly in a state like Massachusetts in which the handling of hides, wool and other animal products is widespread in industry. A letter published elsewhere in this issue of the *Journal* calls attention to the fact that from 1940 to 1945 there were 21 cases of anthrax, with 7 deaths, a mortality of 33 per cent. Furthermore, it appears that the majority of these fatalities could have been avoided if the disease had been recognized at an early date, with the immediate institution of penicillin therapy.[1, 2]

In an attempt to lower the incidence of anthrax, rules and regulations have been adopted that apply to the following industries in which the disease is a hazard: leather manufacturing, wool processing, animal hair and bristle industry, carpet manufacturing, in or in connection with the storage and handling of any animal products (including those of horses and cattle for animal food) and transportation of animal products, such as hides, skins, wool hair, bones, bristles and so forth. These rules and regulations chiefly concern measures to prevent anthrax, such as dust control, the maintenance of clean and sanitary conditions in the plant, and washing facilities, adequate protective covering and individual clothes lockers for employees, as well as a drying room for work clothes. In addition, a responsible plant official is required to arrange for immediate medical attention in all suspected cases, each employee must report any "sore, boil or pimple" and all suspicious lesions must be seen by a designated physician who has "a thorough knowledge of the problems of anthrax." Failure to conform to the statute is punishable by fine.

Undoubtedly most of these requirements have been met for many years by large industrial firms, such as tanneries, in which the employers, employees and company physicians are fully aware of the anthrax hazard. But in small concerns and in those in which the disease occurs infrequently proper precautions have not been taken, and when anthrax has appeared, it has not been diagnosed early enough in the majority of cases for treatment to be as effective as it should be. These new rules and regulations, if properly enforced, should go far in lowering the morbidity and mortality of the disease.

References

1. Murphy, F. D., Boccetta, A. C., and Lockwood, J. S. Treatment of human anthrax with penicillin: report of three cases. *J. A. M. A.* 126:948-950, 1944.
2. Lucchesi, P. F., and Gildersleeve, N. Treatment of anthrax. *J. A. M. A.* 116:1506-1508, 1941.

MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

DAY — Hilbert F. Day, M.D., of Cambridge, died May 16. He was in his sixty-ninth year.

Dr. Day received his degree from Harvard Medical School in 1905. For thirty years he was surgeon-in-chief of the Boston Dispensary. He was a member of the board and a former president of the Washingtonian Hospital and honorary

president of the Cambridge Tuberculosis and Health Association. For twenty years he taught at Harvard Medical School, and since 1934 he had been clinical professor of surgery at Tufts College Medical School. Dr. Day was a member of the New England Obstetrical and Gynecological Society and the New England Pediatric Society and a fellow of the American College of Surgeons and the American Medical Association.

His widow, a son, two daughters, two sisters, a brother and a grandson survive.

HARRIS — Charles E. Harris, M.D., of Hyannis, died May 21. He was in his seventy-ninth year.

Dr. Harris received his degree from Baltimore Medical College in 1897. He served as a major in the Army Medical Corps in World War I.

He is survived by his widow, a son, two daughters and a sister.

KILBURN — Ira N. Kilburn, M.D., of Springfield, died February 2. He was in his sixty-second year.

Dr. Kilburn received his degree from Dartmouth Medical School in 1911. He was a member of the staffs of the Wesson Memorial and Springfield hospitals, and was a member of the American Urological Association.

TOBEY — George L. Tobey, Jr., M.D., of Brookline, died May 20. He was in his sixty-sixth year.

Dr. Tobey received his degree from Harvard Medical School in 1903. He served in World War I as a captain in the Medical Corps. He was a member of the staffs of the Massachusetts General, Boston City, Brooks, New England Deaconess and New England Baptist hospitals and was consulting surgeon at the Massachusetts Eye and Ear Infirmary. He was a former president of the American Otological Society and a former vice-president of the American Academy of Ophthalmology and Oto-Laryngology. He was a member of the American Laryngological Association, American Laryngological, Rhinological and Otological Society and New England Otological and Laryngological Society and a fellow of the American College of Surgeons and the American Medical Association.

His widow, a daughter, a grandson and two brothers survive.

CORRESPONDENCE

PREVENTION OF ANTHRAX

To the Editor: The Massachusetts Department of Labor and Industries has recently passed rules and regulations designed to prevent anthrax in industries where animal products are handled. This step was taken after a survey of these plants by the supervising industrial inspector of the Division of Industrial Safety and the physician of the Division of Occupational Hygiene. The survey followed what might be called an "epidemic" of anthrax among the workers in four relatively small concerns handling hair and wool. Within three years, there were seven cases with four deaths.

Study of collected data shows that in Massachusetts between 1935 and 1940, there were 34 cases of anthrax with 4 deaths, a mortality of 12 per cent; while from 1940 to 1945, there were 21 cases with 7 deaths, a mortality of 33 per cent. Ignorance of the disease on the part of physicians outside those serving in the tanneries of Massachusetts appeared to be the greatest factor in this high mortality rate. Lack of knowledge of the worker and his employer regarding the malignant character of anthrax was also a serious factor. Finally, physicians quite naturally see little of this disease and, in our experience, have been unaware of the heroic measures necessary for its successful treatment. Penicillin, fortunately, appears to be specific therapy if given early and in large doses for a long period.

The following table analyzing the work of the anthrax victims is of importance in bringing out these facts.

Type of Work	No. of Cases	No. of Deaths	Mortality
			%
Tannery	35	1	3
Hair and bristle	7	5	71
Wool	7	3	43
Transportation	4	2	50
Agriculture	2	0	0
	55	11	

Section 9 of the rules and regulations requires the employer to engage a competent physician aware of the anthrax hazard and further to arrange that a worker "with any sore, boil or pimple" on the exposed parts of his body be immediately seen by the designated physician. The remainder of the rules implement this regulation and outline required washing facilities.

Unfortunately, there is no known practical method of destroying anthrax spores in animal products for industrial use without interfering with the commercial value of the material. Animal products imported into this country from the Orient, South America and Europe, notably central European countries, are potential sources of anthrax. Furthermore, recent information from the Veterinary Section of the United States Public Health Service states that anthrax spores occur in the soil and hence on the animals of all but five states in this country, with the heaviest contamination in Texas, Louisiana, South Dakota and California.

There are no interstate quarantine laws for regulating the distribution of anthrax-infected animal products. Federal inspection of imported animal material, formerly carried out by the Bureau of Animal Industry, has been discontinued, since animal anthrax in this country is controlled by anthrax vaccine. Unfortunately, the anthrax vaccine does not rid the animal's hide and hair of anthrax spores, nor is there an anthrax vaccine available for human use.

An understanding of the problem by employer, worker and physician should eliminate fatalities in industries where anthrax is a hazard.

A copy of these rules and regulations may be obtained by writing or phoning the Massachusetts Division of Occupational Hygiene, 286 Congress Street, Boston 10 (phone, LIBerty 0183).

HARRIET L. HARDY, M.D.
Physician, Division of Occupational Hygiene
286 Congress Street
Boston 10

BOND-A-MONTH PLAN

To the Editor: The national debt amounts to $1840 for each man, woman and child in America. The management of this debt will affect prices, employment, wages, how much people can buy and what their savings will be worth. It will affect everyone in his work and at his dinner table.

Wise management of the debt will help level off the economic peaks and valleys that make rough going for all. The Treasury Department, the Federal Reserve Board and the American Bankers Association are unanimously agreed that wise management includes spreading the debt widely, that is, fewer bonds held by banks and more by individuals.

Through the Bond-a-Month Plan, which is currently being announced, the professional man or woman, the business executive and the self-employed are being given the same opportunity for systematic and automatic saving heretofore enjoyed only by industrial employees on payroll savings. Under this plan, commercial banks will invite their depositors, on a card provided by the bank, to direct the bank to make a monthly deduction equivalent to the purchase price of a Series E, F or G Savings Bond. The bank makes the deduction, charges the account for the purchase price and, during the month, mails the bond to the customer. The deductions may be discontinued at any time by authorization.

The plan combines a way to invest regularly in the best possible security and at the same time to help in the wise debt management so essential to the national welfare.

The Bond-a-Month Plan deserves serious consideration. Further details may be obtained at one's bank.

ORVILLE S. POLAND
State Director
U. S. Savings Bonds Division
Treasury Department
79 Milk Street
Boston 9

RESTORATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held May 16, it was voted to restore the registration to practice medicine to Dr. Julius Shubert, 26 Esmond Street, Dorchester, whose registration was revoked June 6, 1945.

H. QUIMBY GALLUPE, M.D., *Secretary*

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held May 16, it was voted to restore the registration to practice medicine to Dr. Aaron O. Bernstein, formerly of 98 Main Street, Gardner, whose registration was revoked June 7, 1945.

H. QUIMBY GALLUPE, M.D., *Secretary*

State House
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Obstetrical Practice. By Alfred C. Beck, M.D., professor of obstetrics and gynecology, Long Island College of Medicine and obstetrician and gynecologist-in-chief, Long Island College Hospital. Fourth edition. 4°, cloth, 966 pp., with 1068 illustrations. Baltimore: Williams and Wilkins Company, 1947. $7.00.

This standard textbook by an outstanding authority in his field, first published in 1935 and translated into Portuguese in 1940, has been revised to bring the text up to date. The sections on implantation and placentation have been rewritten and simplified. The use of penicillin in the prevention of congenital syphilis is discussed in the sections on syphilis and pregnancy and puerperal infection. A new chapter on analgesia, amnesia and anesthesia has been added. The picture of Dr. Oliver Wendell Holmes shows him as an old man. One taken about 1843 would have been more suitable. A list of selected references is appended to each chapter. The text is printed with a good type, and the illustrations are adequate. The price is surprisingly low for the size of the volume. The book is recommended for all medical libraries.

Essentials of Endocrinology. By Arthur Grollman, Ph.D., M.D., professor of medicine and chairman, Department of Experimental Medicine, Southwestern Medical College, and attending physician and consultant in endocrinology, Parkland Hospital, Dallas, Texas. Second edition, revised and enlarged. 8°, cloth, 644 pp., with 132 illustrations. Philadelphia: J. B. Lippincott Company, 1947. $10.00.

This standard work, first published in 1941, has been revised to include new material published during the past six years. Emphasis has been placed on the clinical aspects of endocrinologic disorders in which most of the recent advances have been made.

The material is well organized, and each chapter is documented with a select list of references to the recent literature, analyzed in the text. The book is well published. The type is especially good, and the illustrations are excellent. The volume is heavy for its size, owing to the use of coated paper, and special tables of endocrinologic products are printed on the inside linings of the front and back covers — an unfortunate practice for valuable material. The volume should be in all medical libraries for reference purposes and should prove useful to physicians interested in the subject.

Synopsis of Operative Surgery. By H. E. Mobley, M.D., chief in surgery, St. Anthony's Hospital, Merrilton, Arkansas. Second edition. 8°, cloth, 416 pp., with 383 illustrations, including 37 in color. St. Louis: C. V. Mosby Company, 1947. $6.00.

This manual for students of surgery, first published in 1940, has been revised and brought up to date. The beginning chapters are devoted to anesthesia, postoperative care and surgical technic, and the others to major operations. The drawings are clear and well executed. The material is well arranged and well printed, although the type is small. The manual should prove useful as a reference book for students and surgeons. The price seems excessive for the size of the volume.

The Head, Neck, and Trunk: Muscles and motor points. By Daniel P. Quiring, Ph.D., head of Anatomy Division, Cleveland Clinic Foundation, and associate professor of biology, Western Reserve University. 8°, cloth, 115 pp., with 103 illustrations. Philadelphia: Lea and Febiger, 1947. $2.75.

This small book is designed as a companion volume to the author's *The Extremities*, previously noted in the *Journal*. The individual muscles of the head, neck and trunk are portrayed, together with their chief arterial and nerve supply. The diagrams are excellent and based on original dissections and on references to standard anatomies. The volume should be useful to students and physical therapists, and to surgeons for reference purposes.

Ulcer of the Stomach, Duodenum, and Jejunum. By Ralph C. Brown, M.D., Professor of Medicine, University of Illinois College of Medicine, and attending physician, Presbyterian Hospital, Chicago. 8°, cloth, 172 pp., with 40 illustrations. New York: Oxford University Press, 1946. $2.25. (Reprinted from *Oxford Loose-Leaf Medicine.*)

The author in this small book discusses the pathology, symptoms, diagnosis and treatment of peptic ulcer in the light of the latest knowledge of the subject. Special emphasis is placed on differential diagnosis and treatment. The book should prove useful to physicians in general practice.

Diseases of the Nose and Throat. By Charles J. Imperatori, M.D., consulting laryngologist, Harlem Hospital and Nyack General Hospital, and consulting bronchoscopist, Manhattan Eye, Ear and Throat Hospital, Flower and Fifth Avenue Hospitals, and Riker's Island Hospital; and Herman J. Burman, M.D., director, Department of Otolaryngology, Harlem Hospital, instructor in otolaryngology, Columbia University College of Physicians and Surgeons, and assistant visiting otolaryngologist, Presbyterian Hospital and Vanderbilt Clinic. Third edition. 8°, cloth, 576 pp., with 480 illustrations. Philadelphia: J. B. Lippincott Company, 1947. $12.00.

This standard textbook, first published in 1935 and translated into Spanish in 1942, has been revised to incorporate the advances in the subject since the publication of the second edition in 1939. A new section on the vitamins has been added, and the use of penicillin and the sulfonamides has been discussed especially in relation to intracranial complications. The chapter on radiation therapy has been completely revised and brought up to date. The material is well organized. A two-column format is used to save paper, but the type and printing are good and the volume is well published. The book is recommended to medical libraries as a reference source.

(*Notices on page xvii*)

NOTICES

MEDICAL DIRECTOR FOR RHEUMATIC-FEVER PROGRAM

The Massachusetts Department of Public Health desires to obtain a medical director for its Rheumatic-Fever Program. This medical director will be in charge of the clinical and later the research aspects of the program and will give pediatric support to the rheumatic-fever consultants at the clinics, which initially will be established in the Northeastern Health District (area northeast of Metropolitan Boston).

The medical director will also be in charge of patients hospitalized at North Reading Sanatorium when this institution participates in the program. A close clinical relation between the program and Boston pediatric and rheumatic-fever services will be maintained by the medical director of the program. A vacancy exists at North Reading Sanatorium for this position. The salary is $3480 per year, plus family maintenance.

Qualifications include a pediatric internship, with some experience and interest in rheumatic fever. Interested physicians are requested to communicate with Dr. Florence L. McKay, Director, Division of Maternal and Child Health, 73 Tremont Street, Boston (telephone, CAPitol 4600, extension 271).

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JUNE 12

FRIDAY, JUNE 13

*9:00–10:00 a.m. A Summary of Congenital Heart Disease. Dr. Sidney Farber. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

MONDAY, JUNE 16

*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JUNE 18

*9:00–10:00 a.m. Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*11:00 a.m.–12:00 m. Medical Clinic. Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

JUNE 5–8. American College of Chest Physicians. Page 418, issue of March 13.

JUNE 6–8. American Heart Association. Page xvii, issue of May 8.

JUNE 7 AND 8. American Society for the Study of Sterility. Page 304, issue of February 20.

JUNE 9–13. American Medical Association. Page 698, issue of November 7.

JUNE 11. Harvard Medical Alumni Association. Page 646, issue of April 24.

JUNE 11. Tufts Medical Alumni Dinner. Page 646, issue of April 24.

JUNE 16–18. New England Health Institute. Page 816, issue of May 22.

JUNE 30–JULY 3. American Urological Association. Hotel Statler, Buffalo.

SEPTEMBER 2–6. American Congress of Physical Medicine. Page 610, issue of April 17.

SEPTEMBER 2–7. International Cancer Research Congress. Page 340, issue of February 27.

SEPTEMBER 8–12. Third American Congress on Obstetrics and Gynecology. Page 340, issue of February 27.

OCTOBER 6–10. American Public Health Association. Page 456, issue of March 20.

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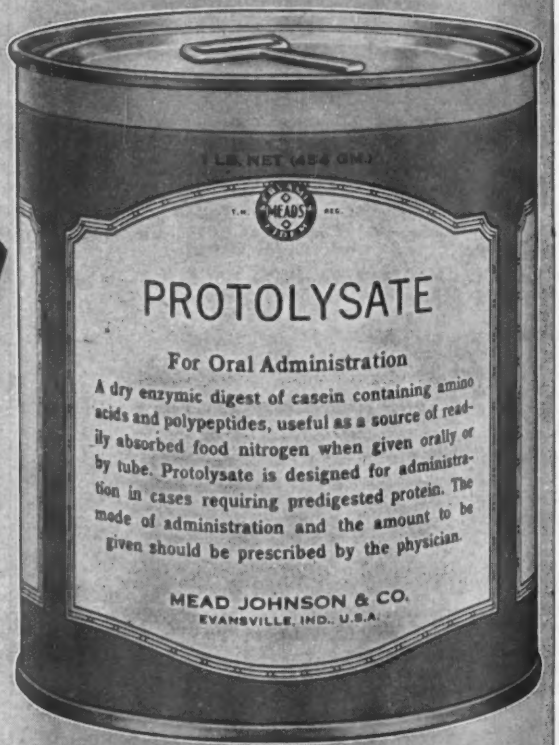
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MEADS
PROTOLYSATE
For Oral Administration
A dry enzymic digest of casein containing amino acids and polypeptides, useful as a source of readily absorbed food nitrogen when given orally or by tube. Protolysate is designed for administration in cases requiring predigested protein. The mode of administration and the amount to be given should be prescribed by the physician.
MEAD JOHNSON & CO.
EVANSVILLE, IND., U.S.A.

COUNCIL-ACCEPTED
PROTOLYSATE
for oral and tube feeding of amino acids

Like Amigen, Protolysate is an enzymic digest of casein and consists of amino acids and polypeptides. Like Amigen, Protolysate supplies the nitrogen essential for maintenance, repair and growth.

Unlike Amigen, which may be employed both orally and parenterally, Protolysate is designed only for oral use.

1 lb. cans at drug stores

MEAD JOHNSON & CO., EVANSVILLE 21, INDIANA

There is no shortage now of AMIGEN for parenteral use. There is no shortage now of PROTOLYSATE for oral use.